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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) **International Patent Classification** 6 : **C12N 15/12, C07K 14/705, A61K 38/17, C12N 5/10, C12Q 1/37, C12N 9/72, 15/85**

A3

(11) **International Publication Number:** **WO 98/55508**

(43) **International Publication Date:** 10 December 1998 (10.12.98)

(21) **International Application Number:** PCT/JP98/02445

(22) **International Filing Date:** 3 June 1998 (03.06.98)

(30) **Priority Data:**
9/144948 3 June 1997 (03.06.97) JP

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(81) **Designated States**: AU, CA, JP, MX, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) **Date of publication of the international search report:**
25 March 1999 (25.03.99)

(54) **Title:** HUMAN PROTEINS HAVING TRANSMEMBRANE DOMAINS AND DNAs ENCODING THESE PROTEINS

(57) **Abstract**

Proteins comprising any of the amino acid sequences of SEQ ID NOS: 1 to 18 and DNAs encoding said proteins and comprising any of the nucelotide sequences of SEQ ID NOS: 19 to 36 are provided.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/JP 98/02445

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C07K14/705 A61K38/17 C12N5/10 C12Q1/37
C12N9/72 C12N15/85

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KYTE J. ET AL.: "A SIMPLE METHOD FOR DISPLAYING THE HYDROPATHIC CHARACTER OF A PROTEIN" JOURNAL OF MOLECULAR BIOLOGY, vol. 157, no. 1, 5 May 1982, pages 105-132, XP000609692 cited in the application ---	
A	LIBERT F. ET AL.: "SELECTIVE AMPLIFICATION AND CLONING OF FOUR NEW MEMBERS OF THE G PROTEIN-COUPLED RECEPTOR FAMILY" SCIENCE, vol. 244, 5 May 1989, pages 569-572, XP002041588 --- -/--	

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

* Special categories of cited documents :

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"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 September 1998	26. 01. 99

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Macchia, G

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

In. .ational application No.
PCT/JP 98/02445

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-6 : all partially (see subject 1, extra sheet)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-6 all partially.

A protein comprising an aminoacid sequence as in Seq.ID:1, encoding DNA, as in Seq.ID19 and 37, related expression vector and transformed eukaryotic cell.

2. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:2, 20 and 38.

3. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:3, 21 and 39.

4. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:4, 22 and 40.

5. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:5, 23 and 41.

6. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:6, 24 and 42.

7. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:7, 25 and 43.

8. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:8, 26 and 44.

9. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:9, 27 and 45.

10. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:10, 28 and 46.

11. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:11, 29 and 47.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

12. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:12, 30 and 48.

13. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:13, 31 and 49.

14. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:14, 32 and 50.

15. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:15, 33 and 51.

16. Claims: 1-6 all partially.

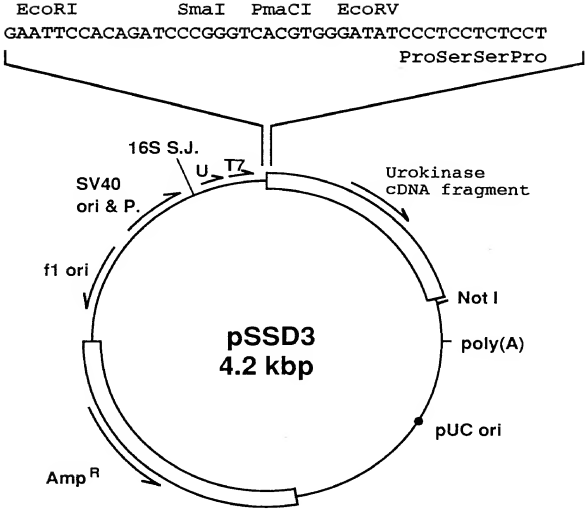
As invention 1 but concerning Seq.ID:16, 34 and 52.

17. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:17, 35 and 53.

18. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:18, 36 and 54.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SV40
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cDNA fragment
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Not I
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pUC ori
Amp R

Fig.1

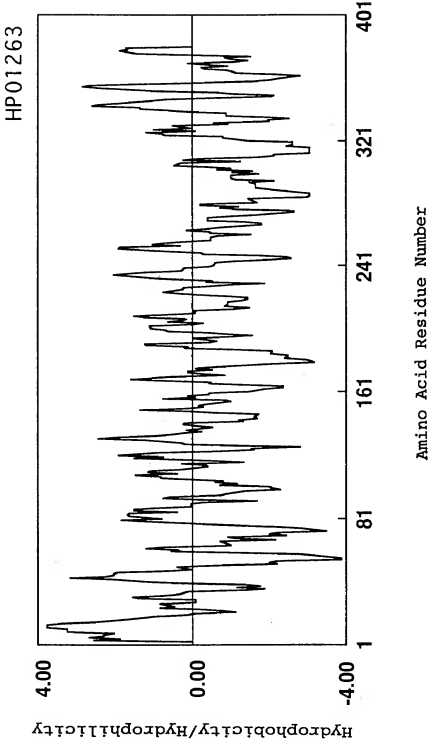
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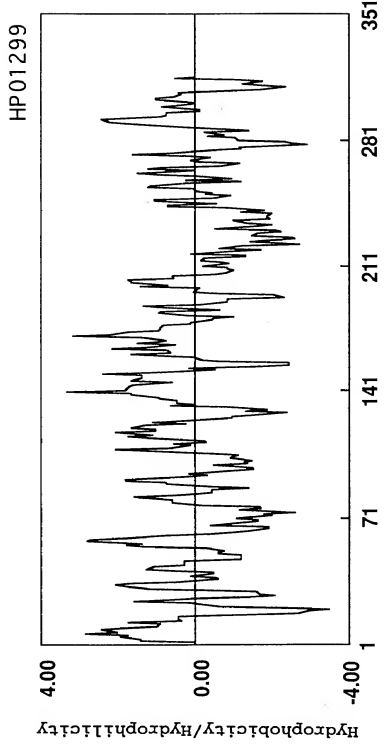
Fig.2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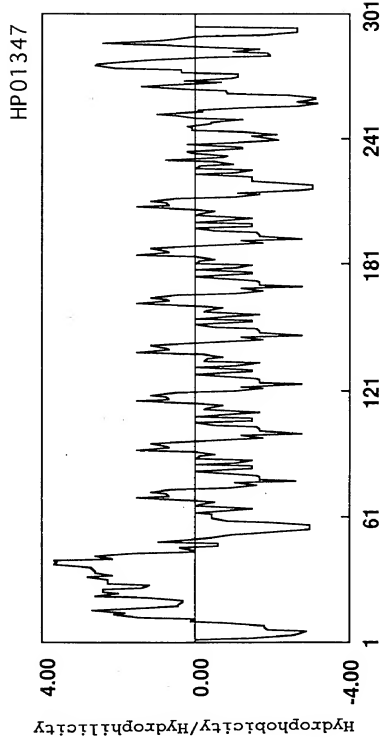
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Fig.4

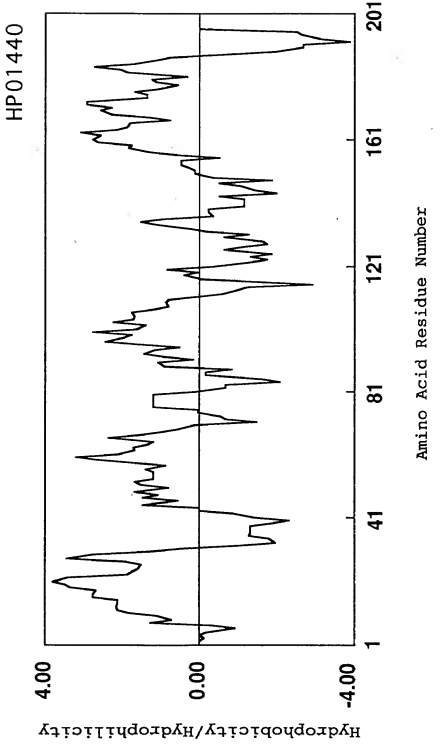
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Fig.5

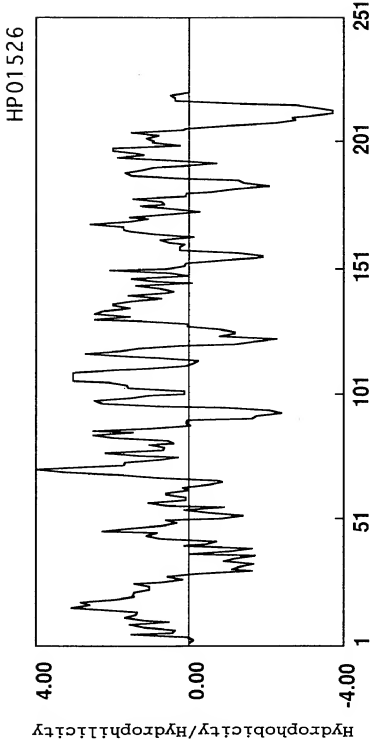
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Fig.6

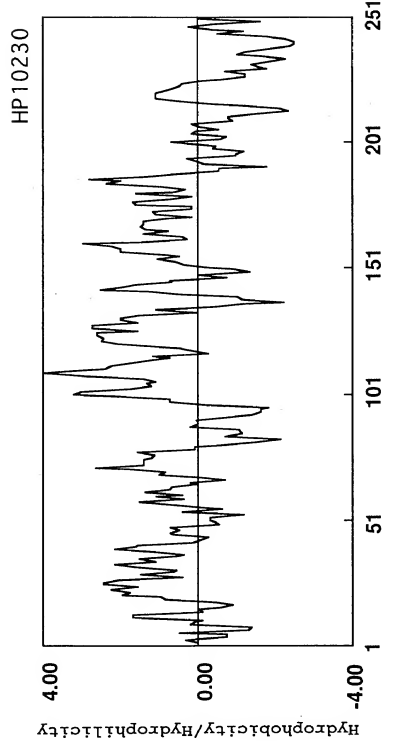
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Fig.7

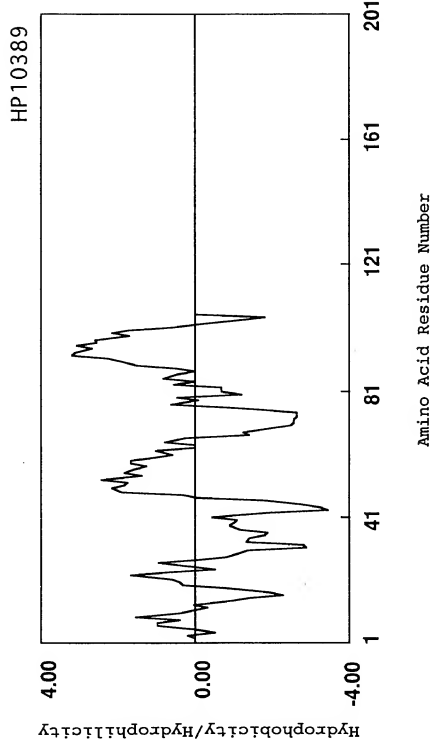
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Fig.8

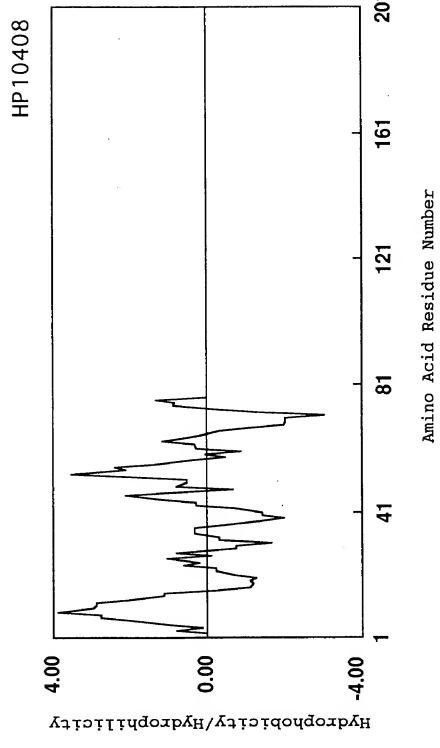
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Fig.9

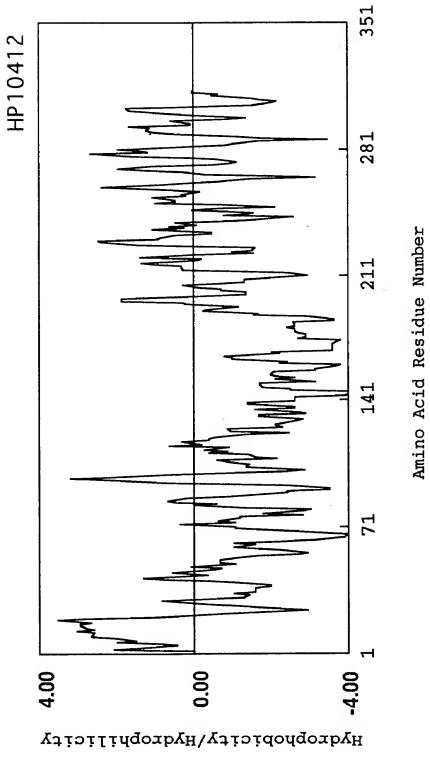
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Fig.10

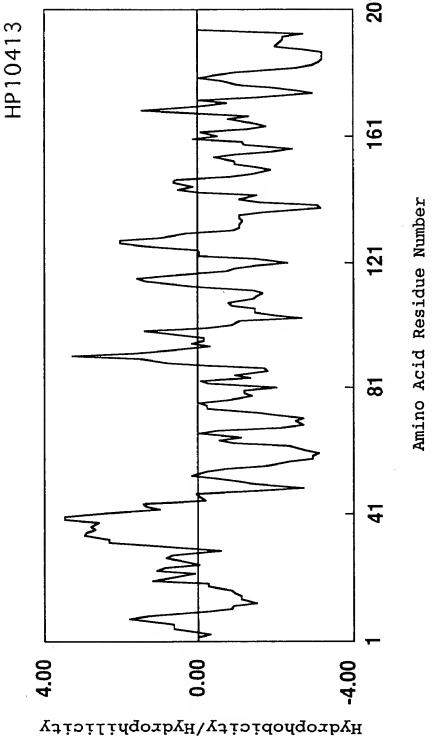
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Fig.11

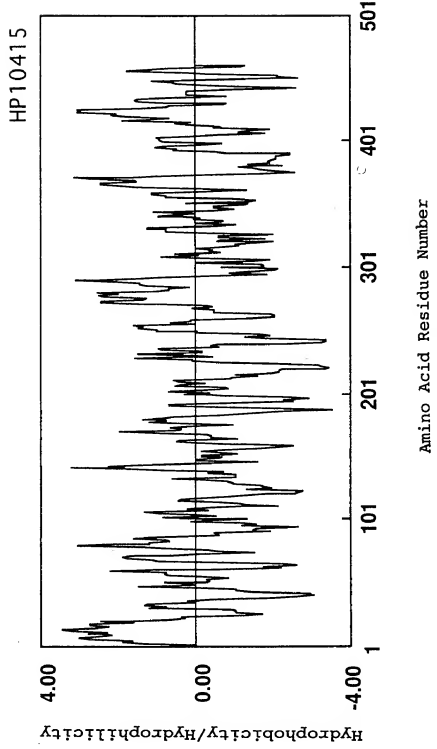
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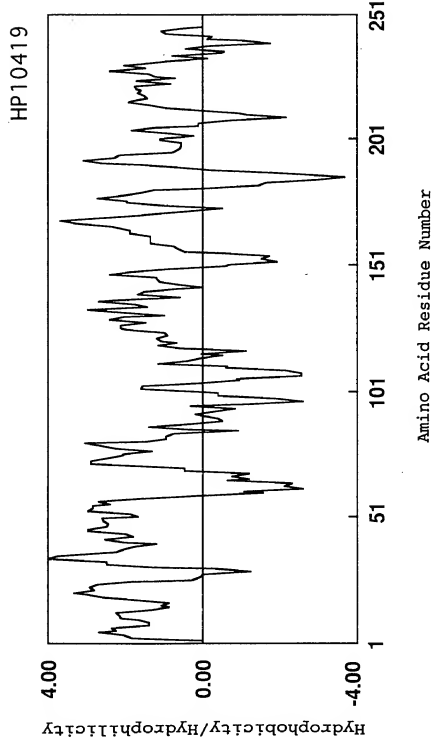
Fig.12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Amino Acid Residue Number

Fig.13

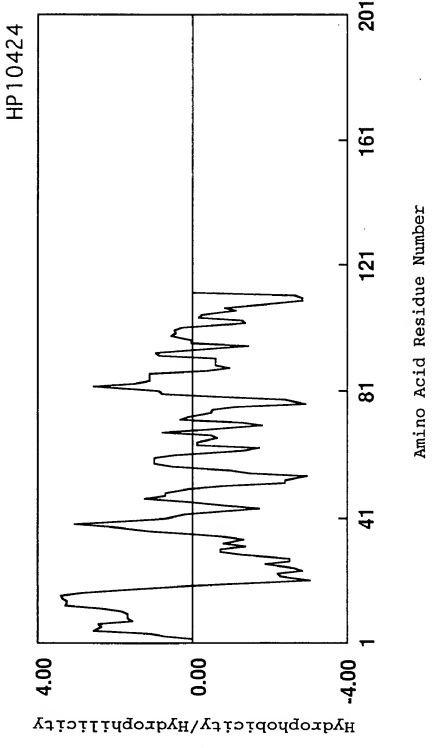
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Fig.14

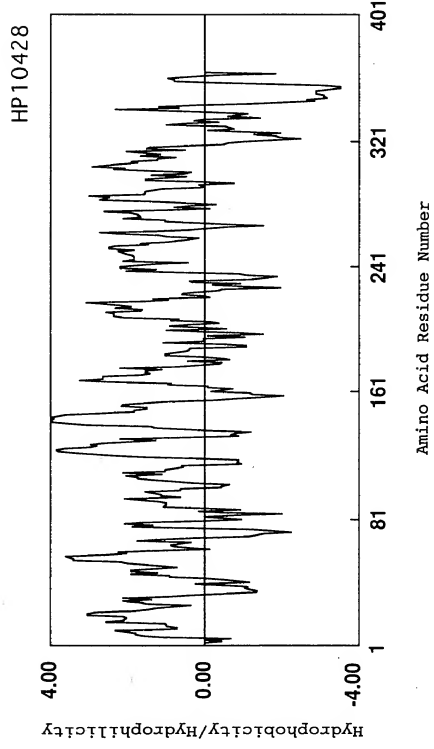
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Fig.15

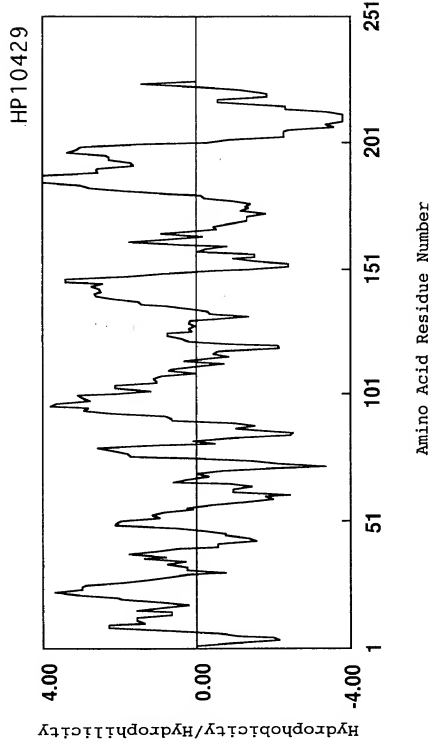
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Fig.16

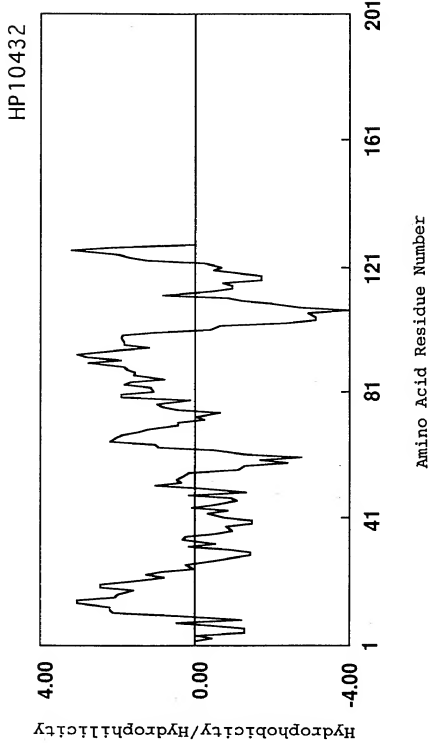
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Fig.17

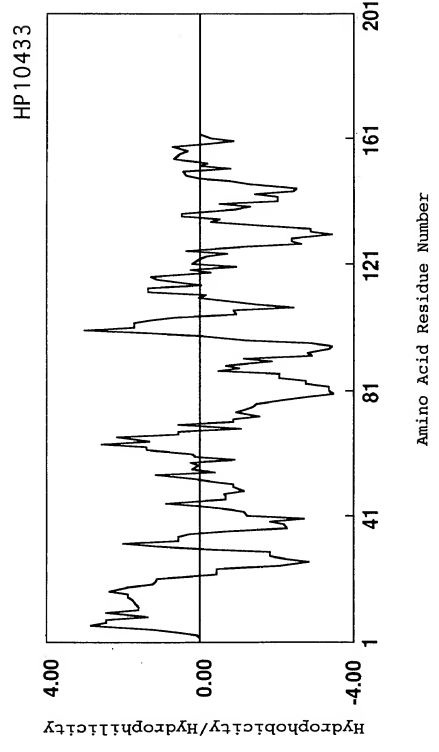
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Fig.18

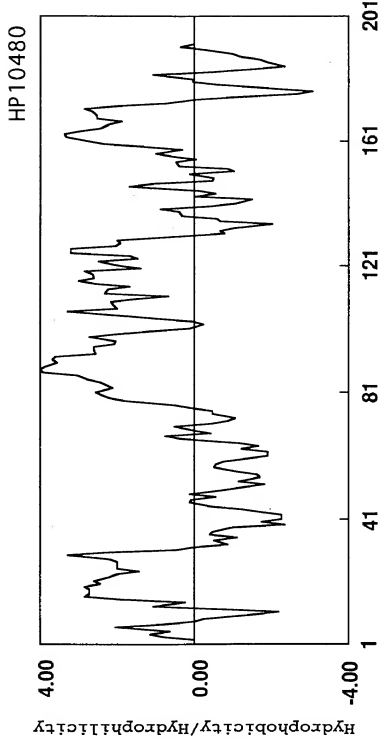
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Fig.19

DESCRIPTION

Human Proteins Having Transmembrane Domains and DNAs Encoding These Proteins

FIELD OF THE INVENTION

The present invention relates to human proteins having transmembrane domains and cDNAs encoding these proteins. The membrane proteins of this invention can be used as pharmaceuticals or as antigens for preparing antibodies against said proteins. The cDNAs of the invention can be used as probes for the gene diagnosis and gene sources for the gene therapy. The cDNAs can also be used as gene sources for large-scale production of the membrane proteins encoded by the same. The cells into which the genes encoding the membrane proteins are introduced for expression of such membrane proteins in large amounts can be used for detection of the corresponding ligands, screening of low molecular weight medicines, etc.

BACKGROUND OF THE INVENTION

Membrane proteins play important roles as signal receptors, ion channels, transporters, etc. for the material transportation or information transmission mediated by the cell membrane. For instance, they are known to serve as receptors for various cytokines, ion channels for sodium ion, potassium ion, chloride ion, etc., transporters for saccharides and amino acids, and so on. The genes for many of them have been cloned already.

In recent years, it was clarified that the abnormalities

of these membrane proteins are related to a number of hitherto cryptogenic diseases. For example, a gene for a membrane protein having 12 transmembrane domains was identified as the gene responsible for cystic fibrosis [Rommens, J. M. et al., Science 245: 1059-1065 (1989)]. It was also clarified that several membrane proteins act as the receptors when a virus infects the cells. For example, HIV-1 was revealed to infect into the cells through the mediation of a membrane protein fusin, a membrane protein on the T-cell membrane, having a CD-4 antigen and 7 transmembrane domains [Feng, Y. et al., Science 272: 872-877 (1996)]. Therefore, the discovery of new membrane proteins is anticipated to lead to the elucidation of the causes of many diseases, and the isolation of new genes coding for the membrane proteins is desired.

Heretofore, owing to the difficulty in their purification, many of membrane proteins have been isolated by an approach from the gene side. A general method is the so-called expression cloning which comprises transfection of a cDNA library in the animal cells to express the cDNA and detection of the cells expressing the target membrane protein on the membrane by an immunological technique using an antibody or a physiological technique for the change in the membrane permeability. However, this method is applicable only to cloning of a gene for a membrane protein with a known function.

In general, membrane proteins possess hydrophobic transmembrane domains inside the proteins which are synthesized in the ribosome. Said domains remain in the phospholipid to be trapped in the membrane. Accordingly, the evidence of the cDNA for encoding the membrane protein is provided by determination

of the whole base sequence of a full-length cDNA and detection of highly hydrophobic transmembrane domains in the amino acid sequence of the protein encoded by said cDNA.

As a result of the extensive study, there have successfully been obtained human proteins having transmembrane domains, particularly comprising any of the amino acid sequences of SEQ ID NOS: 1 to 18, by cloning cDNAs coding for proteins having transmembrane domains, particularly comprising any of the nucleotide sequences of SEQ ID NOS: 19 to 36, from a human full-length cDNA bank. The present invention is based on the above success.

SUMMARY OF THE INVENTION

A main object of the present invention is to provide novel human proteins having transmembrane domains, particularly comprising any of the amino acid sequences of SEQ ID NOS: 1 to 18. Another object of this invention is to provide DNAs coding for said novel proteins, particularly comprising any of the nucleotide sequences of SEQ ID NOS: 19 to 36. A further object of the invention is to provide expression vectors capable of in vitro translating said DNAs or expressing said DNAs in eukaryotic cells. A still further object of the invention is to provide transformed eukaryotic cells capable of expressing said DNAs to produce said proteins.

In one embodiment, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of the amino acid sequences of SEQ ID NOS: 1 to 18 and their fragments.

In another embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 19 to 36.

In a further embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 37 to 54.

BRIEF DESCRIPTION OF DRAWINGS

Figure 1: A figure depicting the structure of the secretory signal sequence detection vector pSSD3.

Figure 2: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01263.

Figure 3: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01299.

Figure 4: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01347.

Figure 5: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01440.

Figure 6: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01526.

Figure 7: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10230.

Figure 8: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10389.

Figure 9: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10408.

Figure 10: A figure depicting the hydrophobicity/hydro-

philicity profile of the protein encoded by clone HP10412.

Figure 11: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10413.

Figure 12: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10415.

Figure 13: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10419.

Figure 14: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10424.

Figure 15: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10428.

Figure 16: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10429.

Figure 17: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10432.

Figure 18: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10433.

Figure 19: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10480.

BEST MODE FOR CARRING OUT INVENTION

The proteins of the present invention can be obtained, for example, by isolation from human organs, cell lines, etc., by chemical synthesis on the basis of the amino acid sequences as herein disclosed, or by recombinant DNA technology using the DNA encoding the transmembrane domains of the invention. Among them, adoption of the recombinant DNA technology is preferred. Specifically, each of the proteins may be prepared by in vitro transcription of a vector comprising the cDNA of the invention

to make RNA and in vitro translation using this RNA as a template to accomplish in vitro expression. Also, each of the proteins may be prepared in a large amount by the use of Escherichia coli, Bacillus subtilis, yeasts, animal cells, etc. comprising a suitable expression vector having the DNA encoding such protein.

In the case of producing the protein of the invention by the use of a microorganism such as Escherichia coli, the translation region of the cDNA of the invention is constructed in an expression vector having an origin, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator, etc. that can be replicated in the microorganism and, after transformation of the host cells with said expression vector, the resultant transformant is incubated, whereby the protein encoded by said cDNA can be produced in a large amount in the microorganism. In that case, a protein fragment containing an optional region can be obtained by performing the expression with inserting an initiation codon and a termination codon before and after the optional translation region. Alternatively, a fusion protein with another protein can be expressed. Only a protein portion encoding said cDNA can be obtained by cleavage of said fusion protein with an appropriate protease.

For production of the protein of the invention by expression of DNA coding for such protein in eukaryotic cells, the translation region of said cDNA may be recombined into an expression vector for eukaryotic cells having a promoter, a splicing domain, a poly(A) addition site, etc., followed by introduction into eukaryotic cells so that the protein of the invention is produced as a membrane protein on the cell

membrane surface. Examples of the expression vector are pKA1, pED6_dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vector, pRS, pYES2, etc. As the eukaryotic cells, there are exemplified mammalian animal culture cells (e.g. simian kidney cells COS7, chinese hamster ovary cells CHO), budding yeasts, Schizosaccharomyces pombe, silkworm cells, Xenopus laevis egg cells, etc., but any other eukaryotic cells may also be used insofar as the protein of the invention can be expressed on the membrane surface. In order to introduce the expression vector into eukaryotic cells, there may be adopted any conventional procedure such as electroporation, calcium phosphate method, liposome method or DEAE dextran method.

The proteins of the present invention include peptide fragments (5 or more amino acid residues) containing any partial amino acid sequence of the amino acid sequences of SEQ ID NOS: 1 to 18. These fragments can be used as antigens for preparation of the antibodies. Also, the proteins of the invention that have signal sequences appear in the form of maturation proteins on the cell surface, after the signal sequences are removed. Therefore, these maturation proteins shall come within the scope of the present invention. The N-terminal amino acid sequences of the maturation proteins can be easily identified by using the method for the cleavage-site determination in a signal sequence [Japan Patent Kokai No. 187100/96]. Further, many membrane proteins are subjected to the processing on the cell surface to be converted to the secretor forms. These secretor proteins or peptides shall come within the scope of the present invention. When glycosylation sites are present in the amino acid sequences, expression in

appropriate animal cells affords glycosylated proteins. Therefore, these glycosylated proteins or peptides also shall come within the scope of the invention.

The DNAs of the invention include all DNAs encoding the above-mentioned proteins. Said DNAs can be obtained using the method by chemical synthesis, the method by cDNA cloning, and so on.

Each of the cDNAs of the invention can be cloned from, for example, the cDNA libraries of the human cell origin. The cDNA is synthesized using as a template a poly(A)$^+$ RNA extracted from human cells. The human cells may be cells delivered from the human body, for example, by the operation or may be the culture cells. The cDNA can be synthesized by using any method selected from the Okayama-Berg method [Okayama, H. and Berg, P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. and Hoffman, J. Gene 25: 263-269 (1983)], and so on, but it is preferred to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)] as illustrated in Examples in order to obtain a full-length clone in an effective manner.

The primary selection of a cDNA encoding a human protein having transmembrane domains is performed by the sequencing of a partial base sequence of the cDNA clone selected at random from the cDNA libraries, sequencing of the amino acid sequence encoded by the base sequence, and recognition of the presence or absence of hydrophobic site(s) in the resulting N-terminal amino acid sequence region. Next, the secondary selection is carried out by determination of the whole base sequence by the sequencing and the protein expression by the in vitro translation. The ascertainment of the cDNA of the present

invention for encoding the protein having the secretory signal sequence is performed by using the signal sequence detection method [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)]. In other words, the ascertainment for the coding portion of the inserted cDNA fragment to function as a signal sequence is provided by fusing a cDNA fragment encoding the N-terminus of the target protein with a cDNA encoding the protease domain of urokinase and then expressing the resulting cDNA in COS7 cells to detect the urokinase activity in the cell culture medium. On the other hand, the N-terminal region is judged to remain in the membrane in the case where the urokinase activity is not detected in the cell culture medium.

The cDNAs of the invention are characterized by containing any of the nucleotide sequences of SEQ ID NOS: 19 to 36 or any of the nucleotide sequences of SEQ ID NOS: 37 to 54. Table 1 summarizes the clone number (HP number), the cells affording the cDNA, the total nucleotide number of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.

Table 1

Sequence Number	HP Number	Cells	Number of Nucleotides	Number of Amino Acid Residues
1, 19, 37	HP01263	Liver	1502	382
2, 20, 38	HP01299	Liver	1349	317
3, 21, 39	HP01347	Liver	1643	296
4, 22, 40	HP01440	Stomach cancer	729	197
5, 23, 41	HP01526	Stomach cancer	1322	221
6, 24, 42	HP10230	Stomach cancer	3045	251
7, 25, 43	HP10389	KB	653	106
8, 26, 44	HP10408	Stomach cancer	439	78
9, 27, 45	HP10412	Stomach cancer	1131	314
10, 28, 46	HP10413	Stomach cancer	1875	195
11, 29, 47	HP10415	Stomach cancer	1563	462
12, 30, 48	HP10419	Stomach cancer	2030	247
13, 31, 49	HP10424	Stomach cancer	493	113
14, 32, 50	HP10428	KB	2044	365
15, 33, 51	HP10429	Stomach cancer	1043	226
16, 34, 52	HP10432	Liver	972	129
17, 35, 53	HP10433	Liver	695	163
18, 36, 54	HP10480	Stomach cancer	1914	193

Hereupon, the same clone as any of the cDNAs of the invention can be easily obtained by screening of the cDNA libraries constructed from the cell line or the human tissues employed in the invention, by the use of an oligonucleotide probe synthesized on the basis of the corresponding cDNA nucleotide sequence of SEQ ID NOS: 37 to 54.

In general, the polymorphism due to the individual difference is frequently observed in human genes. Therefore, any cDNA that is subjected to insertion or deletion of one or plural nucleotides and/or substitution with other nucleotides

in SEQ ID NOS: 37 to 54 shall come within the scope of the invention.

In a similar manner, any protein that is produced by these modifications comprising insertion or deletion of one or plural nucleotides and/or substitution with other nucleotides shall come within the scope of the present invention, as far as said protein possesses the activity of the corresponding protein having the amino acid sequence of SEQ ID NOS: 1 to 18.

The cDNAs of the invention include cDNA fragments (more than 10 bp) containing any partial nucleotide sequence of the nucleotide sequence of SEQ ID NOS: 19 to 36 or of the nucleotide sequence of SEQ ID NOS: 37 to 54. Also, DNA fragments consisting of a sense chain and an anti-sense chain shall come within this scope. These DNA fragments can be used as the probes for the gene diagnosis.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information for identification and/or amplification of genes in appropriate

genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, Trends Pharmacol. Sci. 15(7): 250-254; Lavarosky et al., 1997, Biochem. Mol. Med. 62(1): 11-22; and Hampel, 1998, Prog. Nucleic Acid Res. Mol. Biol. 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished through

insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 396; 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identi fication of molecules that interact with the protein product(s) of the corresponding gene(s).

Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information.

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25%(more preferably at least 50%, and most preferably at

least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

Species homologs of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide, as determined by those of skill in the art. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous, or related to that encoded by the polynucleotides.

The invention also includes polynucleotides with sequences

complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides capable of hybridizing under reduced stringency conditions, more preferably stringent conditions, and most preferably highly stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least as stringent as, for example, conditions M-R.

Table 2

Stringency Condition	Polynucleotide Hybrid	Hybrid Length (bp)‡	Hybridization Temperature and Buffer†	Wash Temperature and Buffer†
A	DNA : DNA	≥50	65℃; 1×SSC -or- 42℃; 1×SSC,50% formamide	65℃; 0.3×SSC
B	DNA : DNA	<50	T_B*; 1×SSC	T_B*; 1×SSC
C	DNA : RNA	≥50	67℃; 1×SSC -or- 45℃; 1×SSC,50% formamide	67℃; 0.3×SSC
D	DNA : RNA	<50	T_D*; 1×SSC	T_D*; 1×SSC
E	RNA : RNA	≥50	70℃; 1×SSC -or- 50℃; 1×SSC,50% formamide	70℃; 0.3×SSC
F	RNA : RNA	<50	T_F*; 1×SSC	T_F*; 1×SSC
G	DNA : DNA	≥50	65℃; 4×SSC -or- 42℃; 4×SSC,50% formamide	65℃; 1×SSC
H	DNA : DNA	<50	T_H*; 4×SSC	T_H*; 4×SSC
I	DNA : RNA	≥50	67℃; 4×SSC -or- 45℃; 4×SSC,50% formamide	67℃; 1×SSC
J	DNA : RNA	<50	T_J*; 4×SSC	T_J*; 4×SSC
K	RNA : RNA	≥50	70℃; 4×SSC -or- 50℃; 4×SSC,50% formamide	67℃; 1×SSC
L	RNA : RNA	<50	T_L*; 2×SSC	T_L*; 2×SSC
M	DNA : DNA	≥50	50℃; 4×SSC -or- 40℃; 6×SSC,50% formamide	50℃; 2×SSC
N	DNA : DNA	<50	T_N*; 6×SSC	T_N*; 6×SSC
O	DNA : RNA	≥50	55℃; 4×SSC -or- 42℃; 6×SSC,50% formamide	55℃; 2×SSC
P	DNA : RNA	<50	T_P*; 6×SSC	T_P*; 6×SSC
Q	RNA : RNA	≥50	60℃; 4×SSC -or- 45℃; 6×SSC,50% formamide	60℃; 2×SSC
R	RNA : RNA	<50	T_R*; 4×SSC	T_R*; 4×SSC

‡ : The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.

† : SSPE (1×SSPE is 0.15M NaCl, 10mM NaH_2PO_4, and 1.25mM EDTA, pH7.4) can be substituted for SSC (1×SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.

*T_B - T_R : The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10℃ less than the melting temperature (T_m) of the hybrid, where T_m is determined according to the following equations. For hybrids less than 18 base pairs in length, T_m(℃)=2(#of A + T bases) + 4(# of G + C bases). For hybrids between 18 and 49 base pairs in length, T_m(℃)=81.5 + 16.6($\log_{10}$[Na^+]) + 0.41 (%G+C) - (600/N), where N is the number of bases in the hybrid, and [Na^+] is the concentration of sodium ions in the hybridization buffer ([Na^+] for 1×SSC=0.165M).

Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and Current Protocols in Molecular Biology, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

Preferably, each such hybridizing polynucleotide has a length that is at least 25%(more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

EXAMPLE

The present invention is embodied in more detail by the following examples, but this embodiment is not intended to restrict the present invention. The basic operations and the enzyme reactions with regard to the DNA recombination are

carried out according to the literature ["Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory, 1989]. Unless otherwise stated, restrictive enzymes and a variety of modification enzymes to be used were those available from Takara Shuzo Co., Ltd. The manufacturer's instructions were used for the buffer compositions as well as for the reaction conditions, in each of the enzyme reactions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

(1) Preparation of Poly(A)$^+$ RNA

The epidermoid carcinoma cell line KB (ATCC CRL 17), tissues of stomach cancer delivered by the operation, and liver were used for human cells to extract mRNAs. The cell line was cultured by a conventional procedure.

After about 1 g of human tissues was homogenized in 20 ml of a 5.5 M guanidinium thiocyanate solution, total mRNAs were prepared in accordance with the literature [Okayama, H. et al., "Methods in Enzymology" Vol. 164, Academic Press, 1987]. These mRNAs were subjected to chromatography using an oligo(dT)-cellulose column washed with 20 mM Tris-hydrochloric acid buffer solution (pH 7.6), 0.5 M NaCl, and 1 mM EDTA to obtain a poly(A)$^+$ RNA in accordance with the above-mentioned literature.

(2) Construction of cDNA Library

To a solution of 10 μg of the above-mentioned poly(A)$^+$ RNA in 100 mM Tris-hydrochloric acid buffer solution (pH 8) was added one unit of an RNase-free, bacterium-origin alkaline phosphatase and the resulting solution was allowed to react at 37°C for one hour. After the reaction solution underwent the

phenol extraction followed by the ethanol precipitation, the obtained pellets were dissolved in a mixed solution of 50 mM sodium acetate (pH 6), 1 mM EDTA, 0.1% 2-mercaptoethanol, and 0.01% Triton X-100. Thereto was added one unit of a tobacco-origin pyrophosphatase (Epicenter Technologies) and the resulting solution at a total volume of 100 µl was allowed to react at 37°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thus-obtained pellets were dissolved in water to obtain a decapped poly(A)$^+$ RNA solution.

To a solution of the decapped poly(A)$^+$ RNA and 3 nmol of a DNA-RNA chimeric oligonucleotide (5'-dG-dG-dG-dG-dA-dA-dT-dT-dC-dG-dA-G-G-A-3') in a mixed aqueous solution of 50 mM Tris-hydrochloric acid buffer solution (pH 7.5), 0.5 mM ATP, 5 mM $MgCl_2$, 10 mM 2-mercaptoethanol, and 25% polyethylene glycol were added 50 units of T4 RNA ligase and the resulting solution at a total volume of 30 µl was allowed to react at 20°C for 12 hours. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thus-obtained pellets were dissolved in water to obtain a chimeric oligo-capped poly(A)$^+$ RNA.

After the vector pKA1 developed by the present inventors (Japanese Patent Kokai Publication No. 1992-117292) was digested with KpnI, an about 60-dT tail was inserted by a terminal transferase. This product was digested with EcoRV to remove the dT tail at one side and the resulting molecule was used as a vectorial primer.

After 6 µg of the previously-prepared chimeric oligo-capped poly(A)$^+$ RNA was annealed with 1.2 µg of the vectorial

primer, the product was dissolved in a mixed solution of 50 mM Tris-hydrochloric acid buffer solution (pH 8.3), 75 mM KCl, 3 mM $MgCl_2$, 10 mM dithiothreitol, and 1.25 mM dNTP (dATP + dCTP + dGTP + dTTP), mixed with 200 units of a reverse transferase (GIBCO-BRL), and the resulting solution at a total volume of 20 µl was allowed to react at 42°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thus-obtained pellets were dissolved in a mixed solution of 50 mM Tris-hydrochloric acid buffer solution (pH 7.5), 100 mM NaCl, 10 mM $MgCl_2$, and 1 mM dithiothreitol. Thereto were added 100 units of EcoRI and the resulting solution at a total volume of 20 µl was allowed to react at 37°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the obtained pellets were dissolved in a mixed solution of 20 mM Tris-hydrochloric acid buffer solution (pH 7.5), 100 mM KCl, 4 mM $MgCl_2$, 10 mM $(NH_4)_2SO_4$, and 50 µg/ml bovine serum albumin. Thereto were added 60 units of *Escherichia coli* DNA ligase and the resulting solution was allowed to react at 16°C for 16 hours. To the reaction solution were added 2 µl of 2 mM dNTP, 4 units of *Escherichia coli* DNA polymerase I, and 0.1 unit of *Escherichia coli* DNase H and the resulting solution was allowed to react at 12°C for one hour and then at 22°C for one hour.

Next, the cDNA-synthesis reaction solution was used to transform *Escherichia coli* DH12S (GIBCO-BRL). The transformation was carried out by the electroporation method. A portion of the transformant was inoculated on a 2xYT agar culture medium containing 100 µg/ml ampicillin, which was

incubated at 37°C overnight. A colony grown on the culture medium was randomly picked up and inoculated on 2 ml of the 2xYT culture medium containing 100 μg/ml ampicillin, which was incubated at 37°C overnight. The culture medium was centrifuged to separate the cells, from which a plasmid DNA was prepared by the alkaline lysis method. After the plasmid DNA was double-digested with EcoRI and NotI, the product was subjected to 0.8% agarose gel electrophoresis to determine the size of the cDNA insert. In addition, by the use of the obtained plasmid as a template, the sequence reaction using M13 universal primer labeled with a fluorescent dye and Taq polymerase (a kit of Applied Biosystems Inc.) was carried out and the product was analyzed by a fluorescent DNA-sequencer (Applied Biosystems Inc.) to determine the base sequence of the cDNA 5′-terminal of about 400 bp. The sequence data were filed as a homo-protein cDNA bank data base.

(3) Selection of cDNAs Encoding Proteins Having Transmembrane Domains

The base sequence registered in the homo-protein cDNA bank data base was converted to three frames of amino acid sequences and the presence or absence of an open reading frame (ORF) beginning from the initiation codon. Then, the selection was made for the presence of a signal sequence that is characteristic to a secretory protein at the N-terminal of the portion encoded by ORF. These clones were sequenced from the both 5′ and 3′ directions by using the deletion method to determine the sequence of the whole base sequence. The hydrophobicity/hydrophilicity profiles were obtained for proteins encoded by ORF by the Kyte-Doolittle method [Kyte, J.

& Doolittle, R. F., J. Mol. Bio. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic region. In the case in which there is a hydrophobic region of putative transmembrane domain(s) in the amino acid sequence of an encoded protein, this protein was considered as a membrane protein.

(4) Construction of Secretory Signal Detection Vector pSSD3

One microgram of pSSD1 carrying the SV40 promoter and a cDNA encoding the protease domain of urokinase [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)] was digested with 5 units of Bg1II and 5 units of EcoRV. Then, after dephosphorylation at the 5' terminal by the CIP treatment, a DNA fragment of about 4.2 kbp was purified by cutting off from the gel of agarose gel electrophoresis.

Two oligo DNA linkers, L1 (5'-GATCCCGGGTCACGTGGGAT-3') and L2 (5'-ATCCCACGTGACCCGG-3'), were synthesized and phosphorylated by T4 polynucleotide kinase. After annealing of the both linkers, followed by ligation with the previously-prepared pSSD1 fragment by T4 DNA ligase, *Escherichia coli* JM109 was transformed. A plasmid pSSD3 was prepared from the transformant and the objective recombinant was confirmed by the determination of the base sequence of the linker-inserted fragment. Figure 1 illustrates the structure of the thus-obtained plasmid. The present plasmid vector carries three types of blunt-end formation restriction enzyme sites, SmaI, PmaCI, and EcoRV. Since these cleavage sites are positioned in succession at an interval of 7 bp, selection of an appropriate site in combination of three types of frames for the inserting

cDNA allows to construct a vector expressing a fusion protein.

(5) Functional Verification of Secretory Signal Sequence

Whether the N-terminal hydrophobic region in the secretory protein clone candidate obtained in the above-mentioned steps functions as the secretory signal sequence was verified by the method described in the literature [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)]. First, the plasmid containing the target cDNA was cleaved at an appropriate restriction enzyme site that existed at the downstream of the portion expected for encoding the secretory signal sequence. In the case in which this restriction enzyme site was a protruding terminus, the site was blunt-ended by the Klenow treatment or treatment with the mung-bean nuclease. Digestion with HindIII was further carried out and a DNA fragment containing the SV40 promoter and a cDNA encoding the secretory sequence at the downstream of the promoter was separated by agarose gel electrophoresis. This fragment was inserted between the pSSD3 HindIII site and a restriction enzyme site selected so as to match with the urokinase-coding frame, thereby constructing a vector expressing a fusion protein of the secretory signal portion of the target cDNA and the urokinase protease domain.

After *Escherichia coli* (host: JM109) bearing the fusion-protein expression vector was incubated at 37°C for 2 hours in 2 ml of the 2xYT culture medium containing 100 μg/ml ampicillin, the helper phage M13KO7 (50 μl) was added and the incubation was continued at 37°C overnight. A supernatant separated by centrifugation underwent precipitation with polyethylene glycol to obtain single-stranded phage particles. These particles were suspended in 100 μl of 1 mM Tris-0.1 mM

EDTA, pH 8 (TE). Also, there was used as a control a suspension of single-stranded particles prepared in the same manner from the vector pLA1-UPA containing pSSD3 and a full-length cDNA of urokinase [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)].

The simian-kidney-origin culture cells, COS7, were incubated at 37°C in the presence of 5% CO_2 in the Dulbecco's modified Eagle's culture medium (DMEM) containing 10% bovine fetus albumin. Into a 6-well plate (Nunc Inc., 3 cm in the well diameter) were inoculated 1×10^5 COS7 cells and incubation was carried out at 37°C for 22 hours in the presence of 5% CO_2. After the culture medium was removed, the cell surface was washed with a phosphate buffer solution and then washed again with DMEM containing 50 mM Tris-hydrochloric acid (pH 7.5) (TDMEM). To the cells were added 1 µl of the single-stranded phage suspension, 0.6 ml of the DMEM culture medium, and 3 µl of TRANSFECTAM™ (IBF Inc.) and the resulting mixture was incubated at 37°C for 3 hours in the presence of 5% CO_2. After the sample solution was removed, the cell surface was washed with TDMEM, 2 ml per well of DMEM containing 10% bovine fetus albumin was added, and the incubation was carried out at 37°C for 2 days in the presence of 5% CO_2.

To 10 ml of 50 mM phosphate buffer solution (pH 7.4) containing 2% bovine fibrinogen (Miles Inc.), 0.5% agarose, and 1 mM potassium chloride were added 10 units of human thrombin (Mochida Pharmaceutical Co., Ltd.) and the resulting mixture was solidified in a plate of 9 cm in diameter to prepare a fibrin plate. Ten microliters of the culture supernatant of the

transfected COS7 cells were spotted on the fibrin plate, which was incubated at 37°C for 15 hours. The diameter of the thus-obtained clear circle was taken as an index for the urokinase activity. In the case in which a cDNA fragment codes for the amino acid sequence that functions as a secretory signal sequence, a fusion protein is secreted to form a clear circle by its urokinase activity. Therefore, in the case in which a clear circle is not formed, the fusion protein remains as trapped in the membrane and the cDNA fragment is considered to code for a transmembrane domain.

(6) Protein Synthesis by In Vitro Translation

The plasmid vector carrying the cDNA of the present invention was utilized for the transcription/translation by the T_NT rabbit reticulocyte lysate kit (Promega Biotec). In this case, [^{35}S]methionine was added and the expression product was labeled with the radioisotope. All reactions were carried out by following the protocols attached to the kit. Two micrograms of the plasmid was allowed to react at 30°C for 90 minutes in total 25 ml of a reaction solution containing 12.5 µl of the T_NT rabbit reticulocyte lysate, 0.5 µl of the buffer solution (attached to the kit), 2 µl of an amino acid mixture (methionine-free), 2 µl (0.37 MBq/µl) of [^{35}S]methionine (Amersham Corporation), 0.5 µl of T7 RNA polymerase, and 20 U of RNasin. To 3 µl of the reaction solution was added 2 µl of an SDS sampling buffer (125 mM Tris-hydrochloric acid suffer solution, pH 6.8, 120 mM 2-mercaptoethanol, 2% SDS solution, 0.025% bromophenol blue, and 20% glycerol) and the resulting solution was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis. The molecular weight of

the translation product was determined by carrying out the autoradiography.

(7) Expression in COS7

Escherichia coli bearing a vector expressing the protein of the invention was infected with helper phage M13KO7, and single-stranded phage particles were obtained according to the method as stated above. Using the thus obtained phages, each expression vecotr was introduced into simian-kidney-origin culture cells COS7 in the manner as stated above. After incubation at 37 °C for 2 days in the presence of 5 % CO_2, further incubation was carried out in a medium containing [^{35}S]cysteine or [^{35}S]methionine for 1 hour. The cells were collected, dissolved and then subjected to SDS-PAGE whereby a band corresponding to the expression product of each protein which is not present in COS7 cells was revealed. In Table 3, the molecular weight of each expression product is shown.

Table 3

HP Number	Supernatant of culture (kDa)	Membrane fraction (kDa)
HP01263	50	-
HP01299	-	30
HP01526	-	22
HP10230	-	24
HP10408	-	7
HP10415	-	45
HP10424	-	14
HP10429	-	27
HP10432	-	17
HP10480	-	22

(8) Clone Examples

<HP01263> (Sequence Number 1, 19, 37)

Determination of the whole base sequence for the cDNA insert of clone HP01263 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-non-translation region of 36 bp, an ORF of 1149 bp, and a 3'-non-translation region of 316 bp. The ORF codes for a protein consisting of 382 amino acid residues with one transmembrane domain at the N-terminal. Figure 2 depicts the hydrophobicity /hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in formation of a translation product of 42 kDa, which is almost consistent with the molecular weight of 42,054 as predicted from the ORF. On expression in COS cells, an expression product of about 50 kDa was observed in the culture supernatant. Therefore, said protein can be understood to be a secreted protein. Application of the rule (-3, -1) as a method for anticipation of a cutting site in a secretion signal sequence suggested that the mature protein would start from methionine at 19 position.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the human α-2-HS-glycoprotein (SWISS-PROT Accession No. P02765). Table 4 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the human α-2-HS-glycoprotein (GP). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the

protein of the present invention. The both proteins possessed a homology of 25.5%. The cysteine position is reserved and this region is analogous to that in cystatins (thiol proteinase inhibitors). There are observed other analogy with histidine-rich glycoprotein (P04196, 30.9%/194 amino acid residues), kininogen (P01045, 24.1%/261 amino acid residues), tyrosine kinase inhibitor (A32827, 24.4%/291 amino acid residues), and so on.

Table 4

```
HP   MGLLLPLALCILVLCCGAMSPPQLALNPSALLSR--GCNDSDVLAVAGFALRDINKDRKD
               .*.** ...   . * . ..*. *  .*.*... ..*  *.  **..
GP         MKSLVLLLCLAQLWGCHSAPHGPGLIYRQPNCDDPETEEAALVAIDYINQNLPW
HP   GYVLRLNRVNDAQEYRRGGLGSLFYLTLDVLETDCHVLRKKAWQDCGMRIFFE-SVYGQC
     **   **...... ...   *.** ...*.***.****  .. . *..* . * .* *.*
GP   GYKHTLNQIDEVKVWPQQPSGELFEIEIDTLETTCHVLDPTPVARCSVRQLKEHAVEGDC
HP   K-AIFYMNNPSRVLYLAAYNCTLRPVSKKKIYMTCPDCPSSIPTDSSNHQVLEAATESLA
     . ... ...  .*.*    .*. .* * ... ..*.***   * .   . .*..**...**
GP   DFQLLKLDGKFSVVY---AKCDSSPDSAEDVRKVCQDCPLLAPLN--DTRVVHAAKAALA
HP   KYNNENTSKQYSLFKVTRASSQWVVGPSYFVEYLIKESPC---TKSQASSCSLQSSDSVP
      .*..*..... * ...**      . ** .**. .... *   . ..*..*.* ...
GP   AFNAQNNGSNFQLEEISRAQLV-PLPPSTYVEFTVSGTDCVAKEATEAAKCNLLAEKQY-
HP   VGLCKGSLTRTHWEKFVSVTCDFFESQAPATGSENSAVNQK-PTNLPKVEESQQKNTPPT
      *.**..*. .  . *.***. *..*. .. .. ...*.  ** . . ....     ..
GP   -GFCKATLSEKLGGAEVAVTCTVFQTQPVTSQPQPEGANEAVPTPVVDPDAPPSPPLGAP
HP   DSPSKAGPRGSVQYLPDLDDKNSQEKGPQEAFPVHLDLTTNPQGETLDISFLFLEPMEEK
     . *. ..*..*   *.
GP   GLPPAGSPPDSHVLLAAPPGHQLHRAHYDLRHTFMGVVSLGSPSGEVSHPRKTRTVVQPS
HP   LVVLPFPKEKARTAECPGPAQNASPLVLPP

GP   VGAAAGPVVPPCPGRIRHFKV
```

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. H57204), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention. Hereupon, most of ESTs matching with the present cDNA are available from liver cDNA libraries, whereby the present clone is considered to be expressed specifically in the liver.

The present protein, because of being a type-II membrane protein, is considered to exert its function as a receptor on the membrane surface with the C-terminal side exposed outside the cells or after undergoing a processing followed by being excreted in the serum. The present protein, because of bearing a cystatin-like domain, is considered to possess a proteinase-inhibitor activity as well as many physiological activities in the same manner as for other members of this family. In addition, the present protein, because of being expressed specifically in liver cells, is considered to play a significant role for maintaining the liver function.

<HP01299> (Sequence Number 2, 20, 38)

Determination of the whole base sequence for the cDNA insert of clone HP01299 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-non-translation region of 110 bp, an ORF of 954 bp, and a 3'-non-translation region of 285 bp. The ORF codes for a protein consisting of 317 amino acid residues with two or more transmembrane domains. Figure 3 depicts the hydrophobicity/hydrophilicity profile of the present protein

obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 32 kDa that was almost consistent with the molecular weight of 35,965 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the rat retinol dehydrogenase (NBRF Accession No. A55884). Table 5 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the rat retinol dehydrogenase (RN). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and. represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 65.3% among the entire regions.

Table 5

```
HP  MWLYLAAFVGLYYLLHWYRERQVVSHLQDKYVFITGCDSGFGNLLARQLDARGLRVLAAC
    ***** *.***. **. .***.**************************** **.******
RN  MWLYLLALVGLWNLLRLFRERKVVSHLQDKYVFITGCDSGFGNLLARQLDRRGMRVLAAC
HP  LTEKGAEQLRGQTSDRLETVTLDVTKMESIAAATQWVKEHVGDRGLWGLVNNAGILTPIT
    **********..********.***** ***.********.**.************ .*..
RN  LTEKGAEQLRSKTSDRLETVILDVTKTESIVAATQWVKERVGNRGLWGLVNNAGISVPVG
HP  LCEWLNTEDSMNMLKVNLIGVIQVTLSMLPLVRRARGRIVNVSSILGRVAFFVGGYCVSK
      **....*  ..*.***.***.***.******.****.**..*..**...  ****.**
RN  PNEWMRKKDFASVLDVNLLGVIEVTLNMLPLVRKARGRVVNIASTMGRMSLVGGGYCISK
HP  YGVEAFSDILRREIQHFGVKISIVEPGYFRTGMTNMTQSLERMKQSWKEAPKHIKETYGQ
    ******** ****. .****..*.*** *.*..***..  ...*. *.......**.**.
RN  YGVEAFSDSLRRELTYFGVKVAIIEPGGFKTNVTNMERLSDNLKKLWDQTTEEVKEIYGE
HP  QYFDALYNIMKEGLLNCSTNLNLVTDCMEHALTSVHPRTRYSAGWDAKFFFIPLSYLPTS
     .. *.  . *.. . .**..*.************ *******.*******..*.*****
RN  KFQDSYMKAMESLVNTCSGDLSLVTDCMEHALTSCHPRTRYSPGWDAKFFYLPMSYLPTF
HP  LADYILTRSWPKPAQAV
    *.* .. ..  ***.*.
RN  LSDAVIHWGSVKPARAL
```

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. R35197), but any of them was shorter than the present cDNA and did not contain the initiation codon.

The rat retinol dehydrogenase has been found as a microsomal membrane protein participating in the retinoic acid

biosynthesis in the liver [Chai, X. et al., J. Biol. Chem. 270: 28408-28412 (1995)]. Accordingly, its homologue, the protein of the present invention, is considered to possess a similar function and can be utilized for diagnosis and treatment of diseases caused by the abnormality of this protein.

<HP01347> (Sequence Number 3, 21, 39)

Determination of the whole base sequence for the cDNA insert of clone HP01347 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-non-translation region of 24 bp, an ORF of 891 bp, and a 3'-non-translation region of 728 bp. The ORF codes for a protein consisting of 296 amino acid residues with one transmembrane domain at the N-terminal. Figure 4 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified and the urokinase activity was detected on the membrane surface, upon transduction into the COS7 cells of an expression vector in which a HindIII-SacI fragment (treated with the mung-bean nuclease) containing a cDNA fragment encoding the N-terminal 73 amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. Therefore, the present protein is considered to be a type-II membrane protein. The in vitro translation resulted in the formation of a translation product of 33 kDa that was almost consistent with the molecular weight of 33,527 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was

analogous to the human HIV envelope glycoprotein gp120-binding C-type lectin (GenBank Accession No. M98457). Table 6 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the human HIV envelope glycoprotein gp120-binding C-type lectin (CL). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 85.6% among 284 amino acid residues. There is observed at the downstream of the transmembrane domain a sequence with seven repetition of Ile-Tyr-Gln-Xaa-Leu-Thr-Xaa-Leu-Lys-Ala-Ala-Val-Gly-Glu-Leu-Xaa-Xaa-Xaa-Ser-Lys-Xaa-Gln-Xaa.

Table 6

```
HP  MSDSKEPRVQQLGLL--------------------GCLGHGALVLQLLSFMLLAGVLVAI
    ********.******                    ******.******** ****    .
CL  MSDSKEPRLQQLGLLEEEQLRGLGFRQTRGYKSLAGCLGHGPLVLQLLSFTLLAG----L
HP  LVQVSKVPSSLSQEQSEQDAIYQNLTQLKAAVGELSEKSKLQEIYQELTQLKAAVGELPE
    **********.****** **********************************************
CL  LVQVSKVPSSISQEQSRQDAIYQNLTQLKAAVGELSEKSKLQEIYQELTQLKAAVGELPE
HP  KSKLQEIYQELTRLKAAVGELPEKSKLQEIYQELTRLKAAVGELPEKSKLQEIYQELTRL
    **********************************.*************.**********
CL  KSKLQEIYQELTRLKAAVGELPEKSKLQEIYQELTWLKAAVGELPEKSKMQEIYQELTRL
HP  KAAVGELPEKSKLQEIYQELTELKAAVGELPEKSKLQEIYQELTQLKAAVGELPDQSKQQ
    ************ ******** ************* ********.*********..****
CL  KAAVGELPEKSKQQEIYQELTRLKAAVGELPEKSKQQEIYQELTRLKAAVGELPEKSKQQ
HP  QIYQELTDLKTAFERLCRHCPKDWTFFQGNCYFMSNSQRNWHDSVTACQEVRAQLVVIKT
    .******.**.* ****..** .**********************.***.** *******.
CL  EIYQELTQLKAAVERLCHPCPWEWTFFQGNCYFMSNSQRNWHDSITACKEVGAQLVVIKS
HP  AEEQLPAVLEQWRTQQ
    ****    *.  *...
CL  AEEQNFLQLQSSRSNRFTWMGLSDLNQEGTWQWVDGSPLLPSFKQYWNRGEPNNVGEEDC
```

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. H90360), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

The present protein, because of being a type-II membrane protein, is considered to exert its function as a receptor on

the membrane surface with the C-terminal side exposed outside the cells or after undergoing a processing followed by being excreted in the serum. Hereupon, the human HIV envelope glycoprotein gp120-binding C-type lectin that is highly homologous with the present protein has been found as a CD4-independent HIV receptor [Curtis, B. M. et al., Proc. Natl. Acad. Sci. USA 89: 8356-8360 (1992)].

<HP01440> (Sequence Number 4, 22, 40)

Determination of the whole base sequence for the cDNA insert of clone HP01440 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 37 bp, an ORF of 594 bp, and a 3'-non-translation region of 98 bp. The ORF codes for a protein consisting of 197 amino acid residues with four transmembrane domains. Figure 5 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 21 kDa that was almost consistent with the molecular weight of 20,822 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the human tumor-associated antigen L6 (SWISS-PROT Accession No. P30408). Table 7 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the human tumor-associated antigen L6 (L6). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed

a homology of 47.0% among the entire regions.

Table 7

```
     HP  MCTGKCARCVGLSLITLCLVCIVANALLLVPNGETSWTNTNHLSLQVWLMGGFIGGGLMV
         ** ******.* **..* *.**.** **  *****.....****  **...*..****..
     L6  MCYGKCARCIGHSLVGLALLCIAANILLYFPNGETKYASENHLSRFVWFFSGIVGGGLLM
     HP  LCPG---IAAVRAGGKGCCGAGCCGNRCRMLRSVFSSAFGVLGAIYCLSVSGAGLRNGPR
         * *.   *.  ...  **** . **.** **.**... .*. *. **. *.. ** .**
     L6  LLPAFVFIGLEQDDCCGCCGHENCGKRCAMLSSVLAALIGIAGSGYCVIVAALGLAEGPL
     HP  CLMN-GEWGYHFEDTAGAYLLNRTLWDRCEAPPRVVPWNVTLFSLLVAASCLEIVLCGIQ
         ** . *.*.* *..*.*.***. . *. *..* ..* ***.***.*.* . .*..** **
     L6  CLDSLGQWNYTFASTEGQYLLDTSTWSECTEPKHIVEWNVSLFSILLALGGIEFILCLIQ
     HP  LVNATICVFCGDCRKKQDTPH
         ..*...* .** * ..*.
     L6  VINGVLGGICGFCCSHQQQYDC
```

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more and also containing the initiation codon (for example, Accession No. T55097), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

The human tumor-associated antigen L6 is a member of a membrane antigen TM4 superfamily proteins which are expressed in large quantities on the surface of human tumor cells [Marken, J. S. et al., Proc. Natl. Acad. Sci. USA 89: 3503-3507 (1992)]. Since these membrane antigens are expressed specifically on some specified cells or cancer cells,

antibodies against these antigens, if constructed, are useful for a variety of diagnoses and as carriers for the drug delivery. In addition, the cells in which genes of these membrane antigens are transduced and the membrane antigens are expressed are applicable for detection of the corresponding ligands and so on.

<HP01526> (Sequence Number 5, 23, 41)

Determination of the whole base sequence for the cDNA insert of clone HP01526 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 83 bp, an ORF of 666 bp, and a 3'-non-translation region of 573 bp. The ORF codes for a protein consisting of 221 amino acid residues with a hydrophobic region of putative six transmembrane domains. Figure 6 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 23 kDa that was almost consistent with the molecular weight of 25,030 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the mouse interstitial cell protein (GenBank Accession No. X96618). Table 8 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the mouse interstitial cell protein (MM). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed

a homology of 79.6% among the entire regions.

Table 8

```
HP  MEAGGFLDSLIYGACVVFTLGMFSAGLSDLRHMRMTRSVDNVQFLPFLTTEVNNLGWLSY
    *****  **.. .***.*******.********..*******.********.****.****
MM  MEAGGVADSFLSSACVLFTLGMFSTGLSDLRHMQRTRSVDNIQFLPFLTTDVNNLSWLSY
HP  GALKGDGILIVVNTVGAALQTLYILAYLHYCPRKRVVLLQTATLLGVLLLGYGYFWLLVP
    *.******.**.**.***.*************.*.*. *********.***************
MM  GVLKGDGTLIIVNSVGAVLQTLYILAYLHYSPQKHGVLLQTATLLAVLLLGYGYFWLLVP
HP  NPEARLQQLGLFCSVFTISMYLSPLADLAKVIQTKSTQCLSYPLTIATLLTSASWCLYGF
    . ****************************..****** **..******. ****..***
MM  DLEARLQQLGLFCSVFTISMYLSPLADLAKIVQTKSTQRLSFSLTIATLFCSASWSIYGF
HP  RLRDPYIMVSNFPGIVTSFIRFWLFWKYPQEQDRNYWLLQT
    ******* *.*.***.**.**. ** ***.****.*.****
MM  RLRDPYIAVPNLPGILTSLIRLGLFCKYPPEQDRKYRLLQT
```

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more and also containing the initiation codon (for example, Accession No. H02682), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

The mouse interstitial cell protein has been cloned as a membrane protein that is expressed with highly increasing in interstitial cells stimulated by a cytokine [Tagoh, H. et al., Biochem. Biophys. Res. Commun. 221: 744-749 (1996)]. Since these membrane proteins are expressed specifically on some specified cells and cancer cells, antibodies against these

proteins, if constructed, are useful for a variety of diagnoses and as carriers for the drug delivery. In addition, the cells in which genes of these membrane antigens are transduced and the membrane antigens are expressed are applicable for detection of the corresponding ligands and so on.

<HP10230> (Sequence Number 6, 24, 42)

Determination of the whole base sequence for the cDNA insert of clone HP10230 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 190 bp, an ORF of 756 bp, and a 3'-non-translation region of 2099 bp. The ORF codes for a protein consisting of 251 amino acid residues with at least one transmembrane domain. Figure 7 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 30 kDa that was almost consistent with the molecular weight of 28,800 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the nematode hypothetical protein F25D7.1 (GenBank Accession No. Z78418). Table 9 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the nematode hypothetical protein F25D7.1 (CE). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 49.8% among the entire regions.

Table 9

```
HS  MSDIGDWFRSIPAITRYWFAATVAVPLVGKLGLISPAYLFL-WPEAFLYRFQIWRPITAT
      *..... .** .***** *.. .**.*..*.*. ...** * .  . .**.***.**
CE   MDLENFLLGIPIVTRYWFLASTIIPLLGRFGFINVQWMFLQW-DLVVNKFQFWRPLTAL
HS  FYFPVGPGTGFLYLVNLYFLYQYSTRLETGAFDGRPADYLFMLLFNW-ICIVITGLAMDM
    .*.**.* *** .*.  ****.**. **.... **.*******.*** .*  .  .*.*.
CE  IYYPVTPQTGFHWLMMCYFLYNYSKALESETYRGRSADYLFMLIFNWFFCSGLC-MALDI
HS  QLLMIPLIMSVLYVWAQLNRDMIVSFWFGTRFKACYLFWVILGFNYIIGGSVINELIGNL
      .*. *...****** *.*.* ******* ** * *****. *** .. *. .***.* *
CE  YFLLEPMVISVLYVWCQVNKDTIVSFWFGMRFPARYLPWVLWGFNAVLRGGGTNELVGIL
HS  VGHLYFFLMFRYPMDLGGRNFLSTPQFLYRWLPSRRGGVSGFGVPPASMRRAADQNGGGG
    *** ***. ..** . *  ...***.**.* .*.  **. *        * *  *  *
CE  VGHAYFFVALKYPDEYGV-DLISTPEFLHRLIPDEDGGIHG---QDGNIRGARQQPRG--
HS  RHNW--GQGFRLGDQ
     * *  * * ***
CE  -HQWPGGVGARLGGN
```

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more and also containing the initiation codon (for example, Accession No. W01493), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

<HP10389> (Sequence Number 7, 25, 43)

Determination of the whole base sequence for the cDNA insert of clone HP10389 obtained from the human epidermoid carcinoma cell line KBc cDNA libraries revealed the structure consisting of a 5'-non-translation region of 62 bp, an ORF of

321 bp, and a 3'-non-translation region of 270 bp. The ORF codes for a protein consisting of 106 amino acid residues with a hydrophobic region of putative two transmembrane domains. Figure 8 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 12 kDa that was almost consistent with the molecular weight of 11,528 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any of known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. H70816), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

<HP10408> (Sequence Number 8, 26, 44)

Determination of the whole base sequence for the cDNA insert of clone HP10408 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 74 bp, an ORF of 237 bp, and a 3'-non-translation region of 128 bp. The ORF codes for a protein consisting of 78 amino acid residues with a putative signal sequence at the N-terminal as well as a sequence of one putative interior transmembrane domain. Figure 9 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified

upon transduction into the COS7 cells of an expression vector in which a HindIII-BglII fragment (after the Klenow treatment) containing a cDNA fragment encoding the N-terminal 70 amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. The in vitro translation resulted in the formation of a translation product of 9 kDa that was almost consistent with the molecular weight of 8,396 predicted from the ORF.

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. T94049), but they were shorter than the present cDNA and any molecule containing the initiation codon was not identified.

<HP10412> (Sequence Number 9, 27, 45)

Determination of the whole base sequence for the cDNA insert of clone HP10412 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 55 bp, an ORF of 945 bp, and a 3'-non-translation region of 131 bp. The ORF codes for a protein consisting of 314 amino acid residues with one transmembrane domain at the N-terminal. Figure 10 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified upon transduction into the COS7 cells of an expression vector in which a HindIII-ApaI fragment (treated with mung-bean nuclease) containing a cDNA fragment encoding the N-terminal 65

amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. The in vitro translation resulted in the formation of a translation product of 44 kDa that was somewhat larger than the molecular weight of 35,610 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the nematode hypothetical protein of 28.5 kDa (SWISS-PROT Accession No. P34623). Table 10 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the nematode hypothetical protein of 28.5 kDa (CE). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 42.8% in the C-terminal region of 243 amino acid residues.

Table 10

```
     HP  MVAPVWYLVAAALLVGFILFLTRSRGRAASAGQEPLHNEELAGAGRVAQPGPLEPEEPRA
     HP  GGRPRRRRDLGSRLQAQRRAQRVAWAEA--DENEEEAVILAQEEEGVEKPAETHLSGKIG
                    * .*.**..* . ...  ..  ...  ... ..*.*. . .. . ***
     CE              MRRNARRRVNRDEQEDGFVNHMMNDGEDVEDLDGGAEQFEYDEDGKKIG
     HP  AKKLRKLEEKQARKAQREAEEAEREERKRLESQREAEWKKEEERLRLEEEQKEEEE--RK
          .*  **..*..... ** *  ******* *..*  * *..*** . *...*.***  **
     CE  KRKAAKLQAKEEKRQMREYEVRERERKRREEER--EKKRDEERAKEEADEKAEEERLRK
     HP  AREEQAQREHEEYLKLKEAFVVEEEGVGETMTEEQSQSFLTEFINYIKQSKVVLLEDLAS
          .***....****** .*..*..**** ......*..... .*..*.* .*** ...*.*
     CE  EREEKERKEHEEYLAMKASFAIEEEG-TDAIEGEEAENLIRDFVDYVKTNKVVNIDELSS
     HP  QVGLRTQDTINRIQDLLAEGTITGVIDDRGKFIYITPEELAAVANFIRQRGRVSIAELAQ
          . **...*..**.*....** . **.*********. **.****.**.******* *.*.
     CE  HFGLKSEDAVNRLQHFIEEGLVQGVMDDRGKFIYISDEEFAAVAKFINQRGRVSIHEIAE
     HP  ASNSLIAWGRESPAQAPA
          .**.**  .  *.*.
     CE  QSNRLIRLETPSAAE
```

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. T09311), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10413> (Sequence Number 10, 28, 46)

Determination of the whole base sequence for the cDNA insert of clone HP10413 obtained from the human stomach cancer

cDNA libraries revealed the structure consisting of a 5'-non-translation region of 78 bp, an ORF of 588 bp, and a 3'-non-translation region of 1209 bp. The ORF codes for a protein consisting of 195 amino acid residues with one transmembrane domain at the N-terminal. Figure 11 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified upon transduction into the COS7 cells of an expression vector in which a HindIII-PmaCI fragment containing a cDNA fragment encoding the N-terminal 65 amino acid residues in the present protein was inserted at the HindIII-PmaCI site of pSSD3. The in vitro translation resulted in the formation of a translation product of 28 kDa that was somewhat larger than the molecular weight of 21,671 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the swine steroidal membrane-binding protein (GenBank Accession No. X99714). Table 11 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the swine steroidal membrane-binding protein (SS). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 96.4% among the entire regions.

Table 11

```
HP  MAAEDVVATGADPSDLESGGLLHEIFTSPLNLLLLGLCIFLLYKIVRGDQPAASGDSDDD
    ******.********.**.************************************ *****
SS  MAAEDVAATGADPSELEGGGLLHEIFTSPLNLLLLGLCIFLLYKIVRGDQPAAS-DSDDD
HP  EPPPLPRLKRRDFTPAELRRFDGVQDPRILMAINGKVFDVTKGRKFYGPEGPYGVFAGRD
    ************************************************************
SS  EPPPLPRLKRRDFTPAELRRFDGVQDPRILMAINGKVFDVTKGRKFYGPEGPYGVFAGRD
HP  ASRGLATFCLDKEALKDEYDDLSDLTAAQQETLSDWESQFTFKYHHVGKLLKEGEEPTVY
    ***************************.*******.**.************************
SS  ASRGLATFCLDKEALKDEYDDLSDLTPAQQETLNDWDSQFTFKYHHVGKLLKEGEEPTVY
HP  SDEEEPKDESARKND
    ***************
SS  SDEEEPKDESARKND
```

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA021062), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

<HP10415> (Sequence Number 11, 29, 47)

Determination of the whole base sequence for the cDNA insert of clone HP10415 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 71 bp, an ORF of 1389 bp, and a 3'-non-translation region of 103 bp. The ORF codes for a protein consisting of 462 amino acid residues with one transmembrane domain at the N-terminal. Figure 12 depicts the hydrophobicity/hydrophilicity profile of the present protein

obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 48 kDa that was somewhat smaller than the molecular weight of 52,458 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the cytochrome P450 as exemplified by the simian cytochrome P450IIIA8 (SWISS-PROT Accession No. P33268). Table 12 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the simian cytochrome P450IIIA8 (CP). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 21.3% among the entire regions.

Table 12

```
    HP    MLDFAIFAVTFLLALVGAVLYLYPASRQAAGIPGITPTEEKDGNLPDIVN-SGSLHEF
                    .***.. ..**** . ...       .*. .    * .*.. . .. .*
 5  CP  MDLIPDLAVETWLLLAVTLVLLYLYGTHSHGLFKKLGIPGPTPLPLLGNILSYRKGFWTF
    HP  LVNLHERYGPVVSFWFGRRLVVSLGTVDVLKQHINPNKTLDPFETMLK-SLLRYQSGGGS
         .. ...** * .*. **. *..... ...*  .  ..  . *...   . . . .. *
    CP  DMECYKKYGKVWGFYDGRQPVLAITDPNMIK-TVLVKECYSVFTNRRPFGPVGFMKNAIS
    HP  VSEN----HMRKKLYENGVTDSLKSNFALLLKLSEELLDKWLSYPET-QHVPLSQHMLGF
10       ..*.    ..*. *  . ....**.  ... * .. *. .  . .** ..*.*.. . ..
    CP  IAEDEEWKRIRSLLSPTFTSGKLKEMVPIIAKYGDVLVRNLRREAETGKPVTLKDVFGAY
    HP  AMKSVTQMVMG----------STF-EDDQEVIRFQKNHGTVWSEIGKGFLDGSLD--KNM
         .*. .*   .*           ..* *......**.  .    * .   *.   *.  .
    CP  SMDVITSTSFGVNIDSLNNPQDPFVENTKKLLRFDFLDPFFLSITIFPFIIPILEVLNIS
15  HP  TRKKQYEDALMQ-LESVLRNIIKE-RKGR-NFSQHIF-----IDSLVQGNLNDQQILEDS
         .  .. .. *.. ....  . .*. .* * .* * ..       ..  . .*.* .....*
    CP  IFPREVTSFLRKSVKRIKESRLKDTQKHRVDFLQLMIDSQNSKETESHKALSDLELVAQS
    HP  MIFSLASCIITAKLCTWAICFLTTSEEVQKKLYEEINQVF-GNGPVTPEKIEQLRYCQHV
         .** .*.. .*... .. *. *.*  .**.** ***. *. ...* * ... *. * . *
20  CP  IIFIFAGYETTSSVLSFIIYELATHPDVQQKLQEEIDTVLPNKAPPTYDTVLQMEYLDMV
    HP  LCETVRTAKLTPVSAQLQDIEGKIDRFIIPRETLVLYALGVVLQDPNTWPSPHKFDPDRF
         . **.*.  ..   ... . . .*. ..**....*. .  .. .**. **.*.** *.**
    HP  VNETLRIFPIAMRLERVCKKDVEINGIFIPKGVVVMIPSYALHHDPKYWPEPEKFLPERF
    HP  ----DDELVMKTFSSLGFSGTQECPELRFAYMVTTVLLSVLVKRLHLLSVEGQVIETKYE
25           .*..   .....* **...* ..*** *  .. .  ..... . . ..  *  *
    CP  SKKNNDNIDPYIYTPFG-SGPRNCIGMRFALMNMKLAIIRVLQNFSFKPCKETQIPLKLR
    HP  LVTSSREEAWITVSKRY
         *
    CP  LGGLLQTEKPIVLKIESRDGTVSGA
30  ____________________________________________________________________
```

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs

possessing the homology of 90% or more (for example, Accession No. AA381169), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

The cytochrome P450 participates in the drug metabolism and can be utilized as a catalyst in organic synthesis reactions such as oxidation and so on.

<HP10419> (Sequence Number 12, 30, 48)

Determination of the whole base sequence for the cDNA insert of clone HP10419 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 170 bp, an ORF of 744 bp, and a 3'-non-translation region of 1116 bp. The ORF codes for a protein consisting of 247 amino acid residues with a hydrophobic region of putative seven transmembrane domains. Figure 13 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method.

The search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA340663), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10424> (Sequence Number 13, 31, 49)

Determination of the whole base sequence for the cDNA insert of clone HP10424 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 97 bp, an ORF of 342 bp, and a 3'-non-translation region of 54 bp. The ORF codes for a protein

consisting of 113 amino acid residues with one transmembrane domain at the N-terminal. Figure 14 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified upon transduction into the COS7 cells of an expression vector in which a HindIII-AccI fragment (after the Klenow treatment) containing a cDNA fragment encoding the N-terminal 58 amino acid residues in the present protein was inserted at the HindIII-SmaI site of pSSD3. The in vitro translation resulted in the formation of a translation product of 14 kDa that was somewhat larger than the molecular weight of 12,784 predicted from the ORF.

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA401979), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10428> (Sequence Number 14, 32, 50)

Determination of the whole base sequence for the cDNA insert of clone HP10428 obtained from the human epidermoid carcinoma cell line KBc cDNA libraries revealed the structure consisting of a 5'-non-translation region of 287 bp, an ORF of 1098 bp, and a 3'-non-translation region of 659 bp. The ORF codes for a protein consisting of 365 amino acid residues with a hydrophobic region of putative nine transmembrane domains. Figure 15 depicts the hydrophobicity/hydrophilicity profile of

the present protein obtained by the Kyte-Doolittle method. The result of the in vitro translation did not reveal the formation of distinct bands and only revealed the formation of smeary bands at the high-molecular-weight position.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the baker's yeast hypothetical membrane protein YML038c (NBRF Accession No. S49741). Table 13 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the baker's yeast hypothetical membrane protein YML038c (SC). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 26.3% among the N-terminal region of 281 amino acid residues.

Table 13

```
      HP  MGRWALDVAFLWKAVLTLGLVL-LYYCFSIGITFYNKWL-----TKSFHFPLFMTMLHLA
                          *..*.  *.*  *....**.*.      . .. .*...* .* *
   5  SC              MNRTVFLAFVFGWYFCS-IALSIYNRWMFDPKDGLGIGYPVLVTTFHQA
      HP  VIFLFSALSRALVQ---CSSHRARVVLSWADYLRRVAPTALATALDVGLSNWSFLYVTVS
          ...*.*..   * .    . * .  ..*. .*. . ***.*.* *.**** ** **...
      SC  TLWLLSGIYIKLRHKPVKNVLRKNNGFNWSFFLKFLLPTAVASAGDIGLSNVSFQYVPLT
      HP  LYTMTKSSAVLFILIFSLIFKLEEL--RAALVLVVLLIAGGLFMF------TYKSTQ-FN
  10       .**..***.. *.*.*. *****..  . ** ....... .*..*       . *..* .
      SC  IYTIIKSSSIAFVLLFGCIFKLEKFHWKLALSVIIMFVGVALMVFKPSDSTSTKNDQALV
      HP  VEGFALVLGASFIGGIRWTLTQMLLQKAELGLQNPIDTMFHLQPLMFLGLFPLFAVFEGL
          . *  ***..* ..*.**. **..*... .  ... ..    .  .* .     .    .
      SC  IFGSFLVLASSCLSGLRWVYTQLMLRNNPIQTNTAAAVEES-DGALFTENEDNVDNEPVV
  15  HP  HLSTSEKIFRFQDT-GLLLRVLGSLFLGGILAFGLGFSEFLLVSRTSSLTLSIAGIFKEV
            .*..... .* ..    ....    *. *....* ... ***... . ..* ..**.
      SC  NLANNKMLENFGESKPHPIHTIHQ--LAPIMGITLLLTS-LLVEKPFPGIFS-SSIFRLD
      HP  CTLLLAAHLLGDQISLLNWLGFALCLSGISLHVALKALHSRGDGGPKALKGLGSSPDLEL

  20  SC  TSNGGVGTETTVLSIVRGIVLLILPGFAVFLLTICEFSILEQTPVLTVSIVGIVKELLTV
      HP  LLRSSQREEGDNEEEEYFVAQGQQ

      SC  IFGIIILSERLSGFYNWLGMLIIMADVCYYNYFRYKQDLLQKYHSVSTQDNRNELKGFQD
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Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA018345), but it can not be assessed whether these ESTs

with partial sequences code for the same protein as the protein of the present invention.

<HP10429> (Sequence Number 15, 33, 51)

Determination of the whole base sequence for the cDNA insert of clone HP10429 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 156 bp, an ORF of 681 bp, and a 3'-non-translation region of 206 bp. The ORF codes for a protein consisting of 226 amino acid residues with four transmembrane domains. Figure 16 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 25 kDa that was almost consistent with the molecular weight of 25,321 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA315933), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10432> (Sequence Number 16, 34, 52)

Determination of the whole base sequence for the cDNA insert of clone HP10429 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-non-translation region of 28 bp, an ORF of 390 bp, and a 3'-non-translation region of 554 bp. The ORF codes for a protein consisting of 129 amino acid residues with a signal-like

sequence at the N-terminal and one interior transmembrane domain. Therefore, the present protein is considered to be a type-I membrane protein. Figure 17 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. T74424), but the same ORF as that in the present cDNA was not identified.

<HP10433> (Sequence Number 17, 35, 53)

Determination of the whole base sequence for the cDNA insert of clone HP10433 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-non-translation region of 72 bp, an ORF of 492 bp, and a 3'-non-translation region of 131 bp. The ORF codes for a protein consisting of 163 amino acid residues with one transmembrane domain at the N-terminal. Figure 18 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified upon transduction into the COS7 cells of an expression vector in which a HindIII-Eco81I fragment (treated with the mung-bean nuclease) containing a cDNA fragment encoding the N-terminal 137 amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. Therefore, the present protein

is considered to be a type-II membrane protein. The in vitro translation resulted in the formation of a translation product of 21 kDa that was almost consistent with the molecular weight of 18,617 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. H84693), but many sequences are not distinct and the same ORF as that in the present cDNA was not identified.

<HP10480> (Sequence Number 18, 36, 54)

Determination of the whole base sequence for the cDNA insert of clone HP10480 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 79 bp, an ORF of 582 bp, and a 3'-non-translation region of 1253 bp. The ORF codes for a protein consisting of 193 amino acid residues with four transmembrane domains. Figure 19 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 23 kDa that was somewhat larger than the molecular weight of 21,445 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or

more (for example, Accession No. W93606), but many sequences are not distinct and the same ORF as that in the present cDNA was not identified.

The present invention provides human proteins having transmembrane domains and cDNAs encoding said proteins. All of the proteins of the present invention are putative proteins controlling the proliferation and differentiation of the cells, because said proteins exist on the cell membrane. Therefore, the proteins of the present invention can be used as pharmaceuticals or as antigens for preparing antibodies against said proteins. Furthermore, said DNAs can be used for the expression of large amounts of said proteins. The cells expressing large amounts of membrane proteins with transfection of these membrane protein genes can be applied to the detection of the corresponding ligands, the screening of novel low-molecular medicines, and so on.

In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

Research Uses and Utilities

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant protein for

analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodiesusing DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in

assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

Nutritional Uses

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source

and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

Cytokine and Cell Proliferation/Differentiation Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H.

Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Po lyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon γ, Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6 -Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et

al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark,S.C. and Turner, K.J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Immune Stimulating or Suppressing Activity

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined

immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial orfungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be

possible to immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2

activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B

lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the commoncold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression

vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I α chain protein and β_2 microglobulin protein or an MHC class IIα chain protein and an MHC class IIβ chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a

T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowmanet al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John

Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in:

Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include,without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

Hematopoiesis Regulating Activity

A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently

of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney,

M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R.E. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

Tissue Growth Activity

A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the

invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue

formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders,

such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon); International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

Activin/Inhibin Activity

A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin α family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin-β group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of

the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

Chemotactic/Chemokinetic Activity

A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell

population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis)consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result,such a protein is expected to be useful in treatment of various coagulation disorders (includinghereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A

protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

Receptor/Ligand Activity

A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors

of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in:Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

Anti-Inflammatory Activity

Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis,

complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of ytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth

Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in

bone form or shape); effecting biorhythms or caricadic cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

CLAIMS

1. A protein comprising an amino acid sequence selected from the group consisting of the amino acid sequences of SEQ ID NOS: 1 to 18.

2. A DNA encoding the protein according to claim 1.

3. A cDNA comprising a nucleotide sequence selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 19 to 36.

4. A cDNA according to claim 3, which comprises a nucleotide sequence selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 37 to 54.

5. An expression vector capable of in vitro translating the DNA according to any of claims 2 to 4 or expressing said DNA in an eukaryotic cell.

6. A transformed eukaryotic cell capable of expressing the DNA according to any of claims 2 to 4 to produce the protein according to claim 1.

add a'

add B'6

Sequence Table

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 382

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Liver

(D) CLONE NAME: HP01263

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

```
Met Gly Leu Leu Leu Pro Leu Ala Leu Cys Ile Leu Val Leu Cys Cys
 1               5                  10                  15
Gly Ala Met Ser Pro Pro Gln Leu Ala Leu Asn Pro Ser Ala Leu Leu
            20                  25                  30
Ser Arg Gly Cys Asn Asp Ser Asp Val Leu Ala Val Ala Gly Phe Ala
        35                  40                  45
Leu Arg Asp Ile Asn Lys Asp Arg Lys Asp Gly Tyr Val Leu Arg Leu
    50                  55                  60
Asn Arg Val Asn Asp Ala Gln Glu Tyr Arg Arg Gly Gly Leu Gly Ser
65                  70                  75                  80
Leu Phe Tyr Leu Thr Leu Asp Val Leu Glu Thr Asp Cys His Val Leu
                85                  90                  95
Arg Lys Lys Ala Trp Gln Asp Cys Gly Met Arg Ile Phe Phe Glu Ser
            100                 105                 110
Val Tyr Gly Gln Cys Lys Ala Ile Phe Tyr Met Asn Asn Pro Ser Arg
        115                 120                 125
Val Leu Tyr Leu Ala Ala Tyr Asn Cys Thr Leu Arg Pro Val Ser Lys
    130                 135                 140
Lys Lys Ile Tyr Met Thr Cys Pro Asp Cys Pro Ser Ser Ile Pro Thr
145                 150                 155                 160
```

SUBSTITUTE SHEET (RULE 26)

Asp Ser Ser Asn His Gln Val Leu Glu Ala Ala Thr Glu Ser Leu Ala
165 170 175
Lys Tyr Asn Asn Glu Asn Thr Ser Lys Gln Tyr Ser Leu Phe Lys Val
180 185 190
Thr Arg Ala Ser Ser Gln Trp Val Val Gly Pro Ser Tyr Phe Val Glu
195 200 205
Tyr Leu Ile Lys Glu Ser Pro Cys Thr Lys Ser Gln Ala Ser Ser Cys
210 215 220
Ser Leu Gln Ser Ser Asp Ser Val Pro Val Gly Leu Cys Lys Gly Ser
225 230 235 240
Leu Thr Arg Thr His Trp Glu Lys Phe Val Ser Val Thr Cys Asp Phe
245 250 255
Phe Glu Ser Gln Ala Pro Ala Thr Gly Ser Glu Asn Ser Ala Val Asn
260 265 270
Gln Lys Pro Thr Asn Leu Pro Lys Val Glu Glu Ser Gln Gln Lys Asn
275 280 285
Thr Pro Pro Thr Asp Ser Pro Ser Lys Ala Gly Pro Arg Gly Ser Val
290 295 300
Gln Tyr Leu Pro Asp Leu Asp Asp Lys Asn Ser Gln Glu Lys Gly Pro
305 310 315 320
Gln Glu Ala Phe Pro Val His Leu Asp Leu Thr Thr Asn Pro Gln Gly
325 330 335
Glu Thr Leu Asp Ile Ser Phe Leu Phe Leu Glu Pro Met Glu Glu Lys
340 345 350
Leu Val Val Leu Pro Phe Pro Lys Glu Lys Ala Arg Thr Ala Glu Cys
355 360 365
Pro Gly Pro Ala Gln Asn Ala Ser Pro Leu Val Leu Pro Pro
370 375 380

(2) INFORMATION FOR SEQ ID NO: 2:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 317
(B) TYPE: Amino acid
(D) TOPOLOGY: Linear
(ii) SEQUENCE KIND: Protein
(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Liver

(D) CLONE NAME: HP01299

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

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            20                  25                  30
Phe Ile Thr Gly Cys Asp Ser Gly Phe Gly Asn Leu Leu Ala Arg Gln
        35                  40                  45
Leu Asp Ala Arg Gly Leu Arg Val Leu Ala Ala Cys Leu Thr Glu Lys
    50                  55                  60
Gly Ala Glu Gln Leu Arg Gly Gln Thr Ser Asp Arg Leu Glu Thr Val
65                  70                  75                  80
Thr Leu Asp Val Thr Lys Met Glu Ser Ile Ala Ala Ala Thr Gln Trp
                85                  90                  95
Val Lys Glu His Val Gly Asp Arg Gly Leu Trp Gly Leu Val Asn Asn
            100                 105                 110
Ala Gly Ile Leu Thr Pro Ile Thr Leu Cys Glu Trp Leu Asn Thr Glu
        115                 120                 125
Asp Ser Met Asn Met Leu Lys Val Asn Leu Ile Gly Val Ile Gln Val
    130                 135                 140
Thr Leu Ser Met Leu Pro Leu Val Arg Arg Ala Arg Gly Arg Ile Val
145                 150                 155                 160
Asn Val Ser Ser Ile Leu Gly Arg Val Ala Phe Phe Val Gly Gly Tyr
                165                 170                 175
Cys Val Ser Lys Tyr Gly Val Glu Ala Phe Ser Asp Ile Leu Arg Arg
            180                 185                 190
Glu Ile Gln His Phe Gly Val Lys Ile Ser Ile Val Glu Pro Gly Tyr
        195                 200                 205
Phe Arg Thr Gly Met Thr Asn Met Thr Gln Ser Leu Glu Arg Met Lys
    210                 215                 220
Gln Ser Trp Lys Glu Ala Pro Lys His Ile Lys Glu Thr Tyr Gly Gln
225                 230                 235                 240
Gln Tyr Phe Asp Ala Leu Tyr Asn Ile Met Lys Glu Gly Leu Leu Asn
```

245 250 255
Cys Ser Thr Asn Leu Asn Leu Val Thr Asp Cys Met Glu His Ala Leu
260 265 270
Thr Ser Val His Pro Arg Thr Arg Tyr Ser Ala Gly Trp Asp Ala Lys
275 280 285
Phe Phe Phe Ile Pro Leu Ser Tyr Leu Pro Thr Ser Leu Ala Asp Tyr
290 295 300
Ile Leu Thr Arg Ser Trp Pro Lys Pro Ala Gln Ala Val
305 310 315

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 296

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Liver

(D) CLONE NAME: HP01347

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

Met Ser Asp Ser Lys Glu Pro Arg Val Gln Gln Leu Gly Leu Leu Gly
1 5 10 15
Cys Leu Gly His Gly Ala Leu Val Leu Gln Leu Leu Ser Phe Met Leu
20 25 30
Leu Ala Gly Val Leu Val Ala Ile Leu Val Gln Val Ser Lys Val Pro
35 40 45
Ser Ser Leu Ser Gln Glu Gln Ser Glu Gln Asp Ala Ile Tyr Gln Asn
50 55 60
Leu Thr Gln Leu Lys Ala Ala Val Gly Glu Leu Ser Glu Lys Ser Lys
65 70 75 80
Leu Gln Glu Ile Tyr Gln Glu Leu Thr Gln Leu Lys Ala Ala Val Gly
85 90 95

Glu Leu Pro Glu Lys Ser Lys Leu Gln Glu Ile Tyr Gln Glu Leu Thr
100 105 110
Arg Leu Lys Ala Ala Val Gly Glu Leu Pro Glu Lys Ser Lys Leu Gln
115 120 125
Glu Ile Tyr Gln Glu Leu Thr Arg Leu Lys Ala Ala Val Gly Glu Leu
130 135 140
Pro Glu Lys Ser Lys Leu Gln Glu Ile Tyr Gln Glu Leu Thr Arg Leu
145 150 155 160
Lys Ala Ala Val Gly Glu Leu Pro Glu Lys Ser Lys Leu Gln Glu Ile
165 170 175
Tyr Gln Glu Leu Thr Glu Leu Lys Ala Ala Val Gly Glu Leu Pro Glu
180 185 190
Lys Ser Lys Leu Gln Glu Ile Tyr Gln Glu Leu Thr Gln Leu Lys Ala
195 200 205
Ala Val Gly Glu Leu Pro Asp Gln Ser Lys Gln Gln Gln Ile Tyr Gln
210 215 220
Glu Leu Thr Asp Leu Lys Thr Ala Phe Glu Arg Leu Cys Arg His Cys
225 230 235 240
Pro Lys Asp Trp Thr Phe Phe Gln Gly Asn Cys Tyr Phe Met Ser Asn
245 250 255
Ser Gln Arg Asn Trp His Asp Ser Val Thr Ala Cys Gln Glu Val Arg
260 265 270
Ala Gln Leu Val Val Ile Lys Thr Ala Glu Glu Gln Leu Pro Ala Val
275 280 285
Leu Glu Gln Trp Arg Thr Gln Gln
290 295

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 197

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP01440

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

```
Met Cys Thr Gly Lys Cys Ala Arg Cys Val Gly Leu Ser Leu Ile Thr
 1               5                  10                  15
Leu Cys Leu Val Cys Ile Val Ala Asn Ala Leu Leu Leu Val Pro Asn
            20                  25                  30
Gly Glu Thr Ser Trp Thr Asn Thr Asn His Leu Ser Leu Gln Val Trp
        35                  40                  45
Leu Met Gly Gly Phe Ile Gly Gly Gly Leu Met Val Leu Cys Pro Gly
    50                  55                  60
Ile Ala Ala Val Arg Ala Gly Gly Lys Gly Cys Cys Gly Ala Gly Cys
65                  70                  75                  80
Cys Gly Asn Arg Cys Arg Met Leu Arg Ser Val Phe Ser Ser Ala Phe
                85                  90                  95
Gly Val Leu Gly Ala Ile Tyr Cys Leu Ser Val Ser Gly Ala Gly Leu
            100                 105                 110
Arg Asn Gly Pro Arg Cys Leu Met Asn Gly Glu Trp Gly Tyr His Phe
        115                 120                 125
Glu Asp Thr Ala Gly Ala Tyr Leu Leu Asn Arg Thr Leu Trp Asp Arg
    130                 135                 140
Cys Glu Ala Pro Pro Arg Val Val Pro Trp Asn Val Thr Leu Phe Ser
145                 150                 155                 160
Leu Leu Val Ala Ala Ser Cys Leu Glu Ile Val Leu Cys Gly Ile Gln
                165                 170                 175
Leu Val Asn Ala Thr Ile Gly Val Phe Cys Gly Asp Cys Arg Lys Lys
            180                 185                 190
Gln Asp Thr Pro His
        195
```

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 221

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:
(A) ORGANISM: *Homo sapiens*
(B) CELL KIND: Stomach cancer
(D) CLONE NAME: HP01526

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

```
Met Glu Ala Gly Gly Phe Leu Asp Ser Leu Ile Tyr Gly Ala Cys Val
 1               5                  10                  15
Val Phe Thr Leu Gly Met Phe Ser Ala Gly Leu Ser Asp Leu Arg His
            20                  25                  30
Met Arg Met Thr Arg Ser Val Asp Asn Val Gln Phe Leu Pro Phe Leu
        35                  40                  45
Thr Thr Glu Val Asn Asn Leu Gly Trp Leu Ser Tyr Gly Ala Leu Lys
    50                  55                  60
Gly Asp Gly Ile Leu Ile Val Val Asn Thr Val Gly Ala Ala Leu Gln
65                  70                  75                  80
Thr Leu Tyr Ile Leu Ala Tyr Leu His Tyr Cys Pro Arg Lys Arg Val
                85                  90                  95
Val Leu Leu Gln Thr Ala Thr Leu Leu Gly Val Leu Leu Leu Gly Tyr
            100                 105                 110
Gly Tyr Phe Trp Leu Leu Val Pro Asn Pro Glu Ala Arg Leu Gln Gln
        115                 120                 125
Leu Gly Leu Phe Cys Ser Val Phe Thr Ile Ser Met Tyr Leu Ser Pro
    130                 135                 140
Leu Ala Asp Leu Ala Lys Val Ile Gln Thr Lys Ser Thr Gln Cys Leu
145                 150                 155                 160
Ser Tyr Pro Leu Thr Ile Ala Thr Leu Leu Thr Ser Ala Ser Trp Cys
                165                 170                 175
Leu Tyr Gly Phe Arg Leu Arg Asp Pro Tyr Ile Met Val Ser Asn Phe
            180                 185                 190
Pro Gly Ile Val Thr Ser Phe Ile Arg Phe Trp Leu Phe Trp Lys Tyr
        195                 200                 205
Pro Gln Glu Gln Asp Arg Asn Tyr Trp Leu Leu Gln Thr
    210                 215                 220
```

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 251

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10230

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

```
Met Ser Asp Ile Gly Asp Trp Phe Arg Ser Ile Pro Ala Ile Thr Arg
 1               5                  10                  15
Tyr Trp Phe Ala Ala Thr Val Ala Val Pro Leu Val Gly Lys Leu Gly
            20                  25                  30
Leu Ile Ser Pro Ala Tyr Leu Phe Leu Trp Pro Glu Ala Phe Leu Tyr
        35                  40                  45
Arg Phe Gln Ile Trp Arg Pro Ile Thr Ala Thr Phe Tyr Phe Pro Val
    50                  55                  60
Gly Pro Gly Thr Gly Phe Leu Tyr Leu Val Asn Leu Tyr Phe Leu Tyr
65                  70                  75                  80
Gln Tyr Ser Thr Arg Leu Glu Thr Gly Ala Phe Asp Gly Arg Pro Ala
                85                  90                  95
Asp Tyr Leu Phe Met Leu Leu Phe Asn Trp Ile Cys Ile Val Ile Thr
            100                 105                 110
Gly Leu Ala Met Asp Met Gln Leu Leu Met Ile Pro Leu Ile Met Ser
        115                 120                 125
Val Leu Tyr Val Trp Ala Gln Leu Asn Arg Asp Met Ile Val Ser Phe
    130                 135                 140
Trp Phe Gly Thr Arg Phe Lys Ala Cys Tyr Leu Pro Trp Val Ile Leu
145                 150                 155                 160
Gly Phe Asn Tyr Ile Ile Gly Gly Ser Val Ile Asn Glu Leu Ile Gly
                165                 170                 175
Asn Leu Val Gly His Leu Tyr Phe Phe Leu Met Phe Arg Tyr Pro Met
```

```
                180                 185                 190
Asp Leu Gly Gly Arg Asn Phe Leu Ser Thr Pro Gln Phe Leu Tyr Arg
        195                 200                 205
Trp Leu Pro Ser Arg Arg Gly Gly Val Ser Gly Phe Gly Val Pro Pro
    210                 215                 220
Ala Ser Met Arg Arg Ala Ala Asp Gln Asn Gly Gly Gly Gly Arg His
225                 230                 235                 240
Asn Trp Gly Gln Gly Phe Arg Leu Gly Asp Gln
                245                 250
```

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 106

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Epidermoid carcinoma

(C) CELL LINE: KB

(D) CLONE NAME: HP10389

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

```
Met Ala Thr Pro Gly Pro Val Ile Pro Glu Val Pro Phe Glu Pro Ser
  1               5                  10                  15
Lys Pro Pro Val Ile Glu Gly Leu Ser Pro Thr Val Tyr Arg Asn Pro
            20                  25                  30
Glu Ser Phe Lys Glu Lys Phe Val Arg Lys Thr Arg Glu Asn Pro Val
        35                  40                  45
Val Pro Ile Gly Cys Leu Ala Thr Ala Ala Ala Leu Thr Tyr Gly Leu
    50                  55                  60
Tyr Ser Phe His Arg Gly Asn Ser Gln Arg Ser Gln Leu Met Met Arg
65                  70                  75                  80
Thr Arg Ile Ala Ala Gln Gly Phe Thr Val Ala Ala Ile Leu Leu Gly
```

85 90 95

Leu Ala Val Thr Ala Met Lys Ser Arg Pro
100 105

(2) INFORMATION FOR SEQ ID NO: 8:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 78
(B) TYPE: Amino acid
(D) TOPOLOGY: Linear
(ii) SEQUENCE KIND: Protein
(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:
(A) ORGANISM: *Homo sapiens*
(B) CELL KIND: Stomach cancer
(D) CLONE NAME: HP10408

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

Met Gly Ser Gly Leu Pro Leu Val Leu Leu Leu Thr Leu Leu Gly Ser
1 5 10 15
Ser His Gly Thr Gly Pro Gly Met Thr Leu Gln Leu Lys Leu Lys Glu
20 25 30
Ser Phe Leu Thr Asn Ser Ser Tyr Glu Ser Ser Phe Leu Glu Leu Leu
35 40 45
Glu Lys Leu Cys Leu Leu Leu His Leu Pro Ser Gly Thr Ser Val Thr
50 55 60
Leu His His Ala Arg Ser Gln His His Val Val Cys Asn Thr
65 70 75

(2) INFORMATION FOR SEQ ID NO: 9:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 314
(B) TYPE: Amino acid
(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10412

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

```
Met Val Ala Pro Val Trp Tyr Leu Val Ala Ala Ala Leu Leu Val Gly
  1               5                  10                  15
Phe Ile Leu Phe Leu Thr Arg Ser Arg Gly Arg Ala Ala Ser Ala Gly
             20                  25                  30
Gln Glu Pro Leu His Asn Glu Glu Leu Ala Gly Ala Gly Arg Val Ala
         35                  40                  45
Gln Pro Gly Pro Leu Glu Pro Glu Glu Pro Arg Ala Gly Gly Arg Pro
     50                  55                  60
Arg Arg Arg Arg Asp Leu Gly Ser Arg Leu Gln Ala Gln Arg Arg Ala
 65                  70                  75                  80
Gln Arg Val Ala Trp Ala Glu Ala Asp Glu Asn Glu Glu Glu Ala Val
                 85                  90                  95
Ile Leu Ala Gln Glu Glu Glu Gly Val Glu Lys Pro Ala Glu Thr His
            100                 105                 110
Leu Ser Gly Lys Ile Gly Ala Lys Lys Leu Arg Lys Leu Glu Glu Lys
        115                 120                 125
Gln Ala Arg Lys Ala Gln Arg Glu Ala Glu Glu Ala Glu Arg Glu Glu
    130                 135                 140
Arg Lys Arg Leu Glu Ser Gln Arg Glu Ala Glu Trp Lys Lys Glu Glu
145                 150                 155                 160
Glu Arg Leu Arg Leu Glu Glu Glu Gln Lys Glu Glu Glu Glu Arg Lys
                165                 170                 175
Ala Arg Glu Glu Gln Ala Gln Arg Glu His Glu Glu Tyr Leu Lys Leu
            180                 185                 190
Lys Glu Ala Phe Val Val Glu Glu Glu Gly Val Gly Glu Thr Met Thr
        195                 200                 205
Glu Glu Gln Ser Gln Ser Phe Leu Thr Glu Phe Ile Asn Tyr Ile Lys
    210                 215                 220
```

Gln Ser Lys Val Val Leu Leu Glu Asp Leu Ala Ser Gln Val Gly Leu
225 230 235 240
Arg Thr Gln Asp Thr Ile Asn Arg Ile Gln Asp Leu Leu Ala Glu Gly
245 250 255
Thr Ile Thr Gly Val Ile Asp Asp Arg Gly Lys Phe Ile Tyr Ile Thr
260 265 270
Pro Glu Glu Leu Ala Ala Val Ala Asn Phe Ile Arg Gln Arg Gly Arg
275 280 285
Val Ser Ile Ala Glu Leu Ala Gln Ala Ser Asn Ser Leu Ile Ala Trp
290 295 300
Gly Arg Glu Ser Pro Ala Gln Ala Pro Ala
305 310

(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 195

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10413

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

Met Ala Ala Glu Asp Val Val Ala Thr Gly Ala Asp Pro Ser Asp Leu
1 5 10 15
Glu Ser Gly Gly Leu Leu His Glu Ile Phe Thr Ser Pro Leu Asn Leu
20 25 30
Leu Leu Leu Gly Leu Cys Ile Phe Leu Leu Tyr Lys Ile Val Arg Gly
35 40 45
Asp Gln Pro Ala Ala Ser Gly Asp Ser Asp Asp Asp Glu Pro Pro Pro
50 55 60
Leu Pro Arg Leu Lys Arg Arg Asp Phe Thr Pro Ala Glu Leu Arg Arg

65 70 75 80
Phe Asp Gly Val Gln Asp Pro Arg Ile Leu Met Ala Ile Asn Gly Lys
85 90 95
Val Phe Asp Val Thr Lys Gly Arg Lys Phe Tyr Gly Pro Glu Gly Pro
100 105 110
Tyr Gly Val Phe Ala Gly Arg Asp Ala Ser Arg Gly Leu Ala Thr Phe
115 120 125
Cys Leu Asp Lys Glu Ala Leu Lys Asp Glu Tyr Asp Asp Leu Ser Asp
130 135 140
Leu Thr Ala Ala Gln Gln Glu Thr Leu Ser Asp Trp Glu Ser Gln Phe
145 150 155 160
Thr Phe Lys Tyr His His Val Gly Lys Leu Leu Lys Glu Gly Glu Glu
165 170 175
Pro Thr Val Tyr Ser Asp Glu Glu Glu Pro Lys Asp Glu Ser Ala Arg
180 185 190
Lys Asn Asp
195

(2) INFORMATION FOR SEQ ID NO: 11:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 462
(B) TYPE: Amino acid
(D) TOPOLOGY: Linear
(ii) SEQUENCE KIND: Protein
(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:
(A) ORGANISM: *Homo sapiens*
(B) CELL KIND: Stomach cancer
(D) CLONE NAME: HP10415

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

Met Leu Asp Phe Ala Ile Phe Ala Val Thr Phe Leu Leu Ala Leu Val
1 5 10 15
Gly Ala Val Leu Tyr Leu Tyr Pro Ala Ser Arg Gln Ala Ala Gly Ile
20 25 30

Pro Gly Ile Thr Pro Thr Glu Glu Lys Asp Gly Asn Leu Pro Asp Ile
35 40 45
Val Asn Ser Gly Ser Leu His Glu Phe Leu Val Asn Leu His Glu Arg
50 55 60
Tyr Gly Pro Val Val Ser Phe Trp Phe Gly Arg Arg Leu Val Val Ser
65 70 75 80
Leu Gly Thr Val Asp Val Leu Lys Gln His Ile Asn Pro Asn Lys Thr
85 90 95
Leu Asp Pro Phe Glu Thr Met Leu Lys Ser Leu Leu Arg Tyr Gln Ser
100 105 110
Gly Gly Gly Ser Val Ser Glu Asn His Met Arg Lys Lys Leu Tyr Glu
115 120 125
Asn Gly Val Thr Asp Ser Leu Lys Ser Asn Phe Ala Leu Leu Leu Lys
130 135 140
Leu Ser Glu Glu Leu Leu Asp Lys Trp Leu Ser Tyr Pro Glu Thr Gln
145 150 155 160
His Val Pro Leu Ser Gln His Met Leu Gly Phe Ala Met Lys Ser Val
165 170 175
Thr Gln Met Val Met Gly Ser Thr Phe Glu Asp Asp Gln Glu Val Ile
180 185 190
Arg Phe Gln Lys Asn His Gly Thr Val Trp Ser Glu Ile Gly Lys Gly
195 200 205
Phe Leu Asp Gly Ser Leu Asp Lys Asn Met Thr Arg Lys Lys Gln Tyr
210 215 220
Glu Asp Ala Leu Met Gln Leu Glu Ser Val Leu Arg Asn Ile Ile Lys
225 230 235 240
Glu Arg Lys Gly Arg Asn Phe Ser Gln His Ile Phe Ile Asp Ser Leu
245 250 255
Val Gln Gly Asn Leu Asn Asp Gln Gln Ile Leu Glu Asp Ser Met Ile
260 265 270
Phe Ser Leu Ala Ser Cys Ile Ile Thr Ala Lys Leu Cys Thr Trp Ala
275 280 285
Ile Cys Phe Leu Thr Thr Ser Glu Glu Val Gln Lys Lys Leu Tyr Glu
290 295 300
Glu Ile Asn Gln Val Phe Gly Asn Gly Pro Val Thr Pro Glu Lys Ile
305 310 315 320
Glu Gln Leu Arg Tyr Cys Gln His Val Leu Cys Glu Thr Val Arg Thr
325 330 335

Ala Lys Leu Thr Pro Val Ser Ala Gln Leu Gln Asp Ile Glu Gly Lys
340 345 350
Ile Asp Arg Phe Ile Ile Pro Arg Glu Thr Leu Val Leu Tyr Ala Leu
355 360 365
Gly Val Val Leu Gln Asp Pro Asn Thr Trp Pro Ser Pro His Lys Phe
370 375 380
Asp Pro Asp Arg Phe Asp Asp Glu Leu Val Met Lys Thr Phe Ser Ser
385 390 395 400
Leu Gly Phe Ser Gly Thr Gln Glu Cys Pro Glu Leu Arg Phe Ala Tyr
405 410 415
Met Val Thr Thr Val Leu Leu Ser Val Leu Val Lys Arg Leu His Leu
420 425 430
Leu Ser Val Glu Gly Gln Val Ile Glu Thr Lys Tyr Glu Leu Val Thr
435 440 445
Ser Ser Arg Glu Glu Ala Trp Ile Thr Val Ser Lys Arg Tyr
450 455 460

(2) INFORMATION FOR SEQ ID NO: 12:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 247

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10419

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

Met Gly Ala Ala Val Phe Phe Gly Cys Thr Phe Val Ala Phe Gly Pro
1 5 10 15
Ala Phe Ala Leu Phe Leu Ile Thr Val Ala Gly Asp Pro Leu Arg Val
20 25 30
Ile Ile Leu Val Ala Gly Ala Phe Phe Trp Leu Val Ser Leu Leu Leu

```
            35                  40                  45
Ala Ser Val Val Trp Phe Ile Leu Val His Val Thr Asp Arg Ser Asp
        50                  55                  60
Ala Arg Leu Gln Tyr Gly Leu Leu Ile Phe Gly Ala Ala Val Ser Val
65                  70                  75                  80
Leu Leu Gln Glu Val Phe Arg Phe Ala Tyr Tyr Lys Leu Leu Lys Lys
                85                  90                  95
Ala Asp Glu Gly Leu Ala Ser Leu Ser Glu Asp Gly Arg Ser Pro Ile
            100                 105                 110
Ser Ile Arg Gln Met Ala Tyr Val Ser Gly Leu Ser Phe Gly Ile Ile
        115                 120                 125
Ser Gly Val Phe Ser Val Ile Asn Ile Leu Ala Asp Ala Leu Gly Pro
    130                 135                 140
Gly Val Val Gly Ile His Gly Asp Ser Pro Tyr Tyr Phe Leu Thr Ser
145                 150                 155                 160
Ala Phe Leu Thr Ala Ala Ile Ile Leu Leu His Thr Phe Trp Gly Val
                165                 170                 175
Val Phe Phe Asp Ala Cys Glu Arg Arg Arg Tyr Trp Ala Leu Gly Leu
            180                 185                 190
Val Val Gly Ser His Leu Leu Thr Ser Gly Leu Thr Phe Leu Asn Pro
        195                 200                 205
Trp Tyr Glu Ala Ser Leu Leu Pro Ile Tyr Ala Val Thr Val Ser Met
    210                 215                 220
Gly Leu Trp Ala Phe Ile Thr Ala Gly Gly Ser Leu Arg Ser Ile Gln
225                 230                 235                 240
Arg Ser Leu Leu Cys Lys Asp
                245
```

(2) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 113

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*
(B) CELL KIND: Stomach cancer
(D) CLONE NAME: HP10424

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

```
Met Asn Phe Tyr Leu Leu Leu Ala Ser Ser Ile Leu Cys Ala Leu Ile
 1               5                  10                  15
Val Phe Trp Lys Tyr Arg Arg Phe Gln Arg Asn Thr Gly Glu Met Ser
            20                  25                  30
Ser Asn Ser Thr Ala Leu Ala Leu Val Arg Pro Ser Ser Ser Gly Leu
        35                  40                  45
Ile Asn Ser Asn Thr Asp Asn Asn Leu Ala Val Tyr Asp Leu Ser Arg
    50                  55                  60
Asp Ile Leu Asn Asn Phe Pro His Ser Ile Ala Arg Gln Lys Arg Ile
65                  70                  75                  80
Leu Val Asn Leu Ser Met Val Glu Asn Lys Leu Val Glu Leu Glu His
                85                  90                  95
Thr Leu Leu Ser Lys Gly Phe Arg Gly Ala Ser Pro His Arg Lys Ser
            100                 105                 110
Thr
```

(2) INFORMATION FOR SEQ ID NO: 14:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 365
(B) TYPE: Amino acid
(D) TOPOLOGY: Linear
(ii) SEQUENCE KIND: Protein
(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:
(A) ORGANISM: *Homo sapiens*
(B) CELL KIND: Epidermoid carcinoma
(C) CELL LINE: KB
(D) CLONE NAME: HP10428

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

```
Met Gly Arg Trp Ala Leu Asp Val Ala Phe Leu Trp Lys Ala Val Leu
 1               5                  10                  15
Thr Leu Gly Leu Val Leu Leu Tyr Tyr Cys Phe Ser Ile Gly Ile Thr
            20                  25                  30
Phe Tyr Asn Lys Trp Leu Thr Lys Ser Phe His Phe Pro Leu Phe Met
        35                  40                  45
Thr Met Leu His Leu Ala Val Ile Phe Leu Phe Ser Ala Leu Ser Arg
    50                  55                  60
Ala Leu Val Gln Cys Ser Ser His Arg Ala Arg Val Val Leu Ser Trp
65                  70                  75                  80
Ala Asp Tyr Leu Arg Arg Val Ala Pro Thr Ala Leu Ala Thr Ala Leu
                85                  90                  95
Asp Val Gly Leu Ser Asn Trp Ser Phe Leu Tyr Val Thr Val Ser Leu
            100                 105                 110
Tyr Thr Met Thr Lys Ser Ser Ala Val Leu Phe Ile Leu Ile Phe Ser
        115                 120                 125
Leu Ile Phe Lys Leu Glu Glu Leu Arg Ala Ala Leu Val Leu Val Val
    130                 135                 140
Leu Leu Ile Ala Gly Gly Leu Phe Met Phe Thr Tyr Lys Ser Thr Gln
145                 150                 155                 160
Phe Asn Val Glu Gly Phe Ala Leu Val Leu Gly Ala Ser Phe Ile Gly
                165                 170                 175
Gly Ile Arg Trp Thr Leu Thr Gln Met Leu Leu Gln Lys Ala Glu Leu
            180                 185                 190
Gly Leu Gln Asn Pro Ile Asp Thr Met Phe His Leu Gln Pro Leu Met
        195                 200                 205
Phe Leu Gly Leu Phe Pro Leu Phe Ala Val Phe Glu Gly Leu His Leu
    210                 215                 220
Ser Thr Ser Glu Lys Ile Phe Arg Phe Gln Asp Thr Gly Leu Leu Leu
225                 230                 235                 240
Arg Val Leu Gly Ser Leu Phe Leu Gly Gly Ile Leu Ala Phe Gly Leu
                245                 250                 255
Gly Phe Ser Glu Phe Leu Leu Val Ser Arg Thr Ser Ser Leu Thr Leu
            260                 265                 270
Ser Ile Ala Gly Ile Phe Lys Glu Val Cys Thr Leu Leu Leu Ala Ala
        275                 280                 285
His Leu Leu Gly Asp Gln Ile Ser Leu Leu Asn Trp Leu Gly Phe Ala
    290                 295                 300
```

Leu Cys Leu Ser Gly Ile Ser Leu His Val Ala Leu Lys Ala Leu His
305 310 315 320

Ser Arg Gly Asp Gly Gly Pro Lys Ala Leu Lys Gly Leu Gly Ser Ser
325 330 335

Pro Asp Leu Glu Leu Leu Leu Arg Ser Ser Gln Arg Glu Glu Gly Asp
340 345 350

Asn Glu Glu Glu Glu Tyr Phe Val Ala Gln Gly Gln Gln
355 360 365

(2) INFORMATION FOR SEQ ID NO: 15:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 226

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10429

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

Met Pro Thr Thr Lys Lys Thr Leu Met Phe Leu Ser Ser Phe Phe Thr
1 5 10 15

Ser Leu Gly Ser Phe Ile Val Ile Cys Ser Ile Leu Gly Thr Gln Ala
20 25 30

Trp Ile Thr Ser Thr Ile Ala Val Arg Asp Ser Ala Ser Asn Gly Ser
35 40 45

Ile Phe Ile Thr Tyr Gly Leu Phe Arg Gly Glu Ser Ser Glu Glu Leu
50 55 60

Ser His Gly Leu Ala Glu Pro Lys Lys Lys Phe Ala Val Leu Glu Ile
65 70 75 80

Leu Asn Asn Ser Ser Gln Lys Thr Leu His Ser Val Thr Ile Leu Phe
85 90 95

Leu Val Leu Ser Leu Ile Thr Ser Leu Leu Ser Ser Gly Phe Thr Phe

100 105 110
Tyr Asn Ser Ile Ser Asn Pro Tyr Gln Thr Phe Leu Gly Pro Thr Gly
115 120 125
Val Tyr Thr Trp Asn Gly Leu Gly Ala Ser Phe Val Phe Val Thr Met
130 135 140
Ile Leu Phe Val Ala Asn Thr Gln Ser Asn Gln Leu Ser Glu Glu Leu
145 150 155 160
Phe Gln Met Leu Tyr Pro Ala Thr Thr Ser Lys Gly Thr Thr His Ser
165 170 175
Tyr Gly Tyr Ser Phe Trp Leu Ile Leu Leu Val Ile Leu Leu Asn Ile
180 185 190
Val Thr Val Thr Ile Ile Ile Phe Tyr Gln Lys Ala Arg Tyr Gln Arg
195 200 205
Lys Gln Glu Gln Arg Lys Pro Met Glu Tyr Ala Pro Arg Asp Gly Ile
210 215 220
Leu Phe
225

(2) INFORMATION FOR SEQ ID NO: 16:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 129
(B) TYPE: Amino acid
(D) TOPOLOGY: Linear
(ii) SEQUENCE KIND: Protein
(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:
(A) ORGANISM: *Homo sapiens*
(B) CELL KIND: Liver
(D) CLONE NAME: HP10432

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

Met Ala Arg Gly Ser Leu Arg Arg Leu Leu Arg Leu Leu Val Leu Gly
1 5 10 15
Leu Trp Leu Ala Leu Leu Arg Ser Val Ala Gly Glu Gln Ala Pro Gly
20 25 30

Thr Ala Pro Cys Ser Arg Gly Ser Ser Trp Ser Ala Asp Leu Asp Lys
35 40 45
Cys Met Asp Cys Ala Ser Cys Arg Ala Arg Pro His Ser Asp Phe Cys
50 55 60
Leu Gly Cys Ala Ala Ala Pro Pro Ala Pro Phe Arg Leu Leu Trp Pro
65 70 75 80
Ile Leu Gly Gly Ala Leu Ser Leu Thr Phe Val Leu Gly Leu Leu Ser
85 90 95
Gly Phe Leu Val Trp Arg Arg Cys Arg Arg Arg Glu Lys Phe Thr Thr
100 105 110
Pro Ile Glu Glu Thr Gly Gly Glu Gly Cys Pro Ala Val Ala Leu Ile
115 120 125
Gln

(2) INFORMATION FOR SEQ ID NO: 17:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 163

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Liver

(D) CLONE NAME: HP10433

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

Met Arg Arg Leu Leu Ile Pro Leu Ala Leu Trp Leu Gly Ala Val Gly
1 5 10 15
Val Gly Val Ala Glu Leu Thr Glu Ala Gln Arg Arg Gly Leu Gln Val
20 25 30
Ala Leu Glu Glu Phe His Lys His Pro Pro Val Gln Trp Ala Phe Gln
35 40 45
Glu Thr Ser Val Glu Ser Ala Val Asp Thr Pro Phe Pro Ala Gly Ile

```
     50                  55                  60
Phe Val Arg Leu Glu Phe Lys Leu Gln Gln Thr Ser Cys Arg Lys Arg
 65                  70                  75                  80
Asp Trp Lys Lys Pro Glu Cys Lys Val Arg Pro Asn Gly Arg Lys Arg
                85                  90                  95
Lys Cys Leu Ala Cys Ile Lys Leu Gly Ser Glu Asp Lys Val Leu Gly
            100                 105                 110
Arg Leu Val His Cys Pro Ile Glu Thr Gln Val Leu Arg Glu Ala Glu
        115                 120                 125
Glu His Gln Glu Thr Gln Cys Leu Arg Val Gln Arg Ala Gly Glu Asp
    130                 135                 140
Pro His Ser Phe Tyr Phe Pro Gly Gln Phe Ala Phe Ser Lys Ala Leu
145                 150                 155                 160
Pro Arg Ser
```

(2) INFORMATION FOR SEQ ID NO: 18:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 193

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10480

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

```
Met Ile Arg Cys Gly Leu Ala Cys Glu Arg Cys Arg Trp Ile Leu Pro
 1               5                  10                  15
Leu Leu Leu Leu Ser Ala Ile Ala Phe Asp Ile Ile Ala Leu Ala Gly
            20                  25                  30
Arg Gly Trp Leu Gln Ser Ser Asp His Gly Gln Thr Ser Ser Leu Trp
        35                  40                  45
Trp Lys Cys Ser Gln Glu Gly Gly Gly Ser Gly Ser Tyr Glu Glu Gly
```

```
     50                  55                  60
Cys Gln Ser Leu Met Glu Tyr Ala Trp Gly Arg Ala Ala Ala Ala Met
 65                  70                  75                  80
Leu Phe Cys Gly Phe Ile Ile Leu Val Ile Cys Phe Ile Leu Ser Phe
                85                  90                  95
Phe Ala Leu Cys Gly Pro Gln Met Leu Val Phe Leu Arg Val Ile Gly
            100                 105                 110
Gly Leu Leu Ala Leu Ala Ala Val Phe Gln Ile Ile Ser Leu Val Ile
        115                 120                 125
Tyr Pro Val Lys Tyr Thr Gln Thr Phe Thr Leu His Ala Asn Arg Ala
    130                 135                 140
Val Thr Tyr Ile Tyr Asn Trp Ala Tyr Gly Phe Gly Trp Ala Ala Thr
145                 150                 155                 160
Ile Ile Leu Ile Gly Cys Ala Phe Phe Phe Cys Cys Leu Pro Asn Tyr
                165                 170                 175
Glu Asp Asp Leu Leu Gly Asn Ala Lys Pro Arg Tyr Phe Tyr Thr Ser
            180                 185                 190
Ala
```

(2) INFORMATION FOR SEQ ID NO: 19:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1146

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Linear

(D) CLONE NAME: HP01263

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

```
ATGGGTCTGC TCCTTCCCCT GGCACTCTGC ATCCTAGTCC TGTGCTGCGG AGCAATGTCT     60
CCACCCCAGC TGGCCCTCAA CCCCTCGGCT CTGCTCTCCC GGGGCTGCAA TGACTCCGAT    120
GTGCTGGCAG TTGCAGGCTT TGCCCTGCGG GATATTAACA AAGACAGAAA GGATGGCTAT    180
```

GTGCTGAGAC TCAACCGAGT GAACGACGCC CAGGAATACA GACGGGGTGG CCTGGGATCT 240
CTGTTCTATC TTACACTGGA TGTGCTAGAG ACTGACTGCC ATGTGCTCAG AAAGAAGGCA 300
TGGCAAGACT GTGGAATGAG GATATTTTTT GAATCAGTTT ATGGTCAATG CAAAGCAATA 360
TTTTATATGA ACAACCCAAG TAGAGTTCTC TATTTAGCTG CTTATAACTG TACTCTTCGC 420
CCAGTTTCAA AAAAAAAGAT TTACATGACG TGCCCTGACT GCCCAAGCTC CATACCCACT 480
GACTCTTCCA ATCACCAAGT GCTGGAGGCT GCCACCGAGT CTCTTGCGAA ATACAACAAT 540
GAGAACACAT CCAAGCAGTA TTCTCTCTTC AAAGTCACCA GGGCTTCTAG CCAGTGGGTG 600
GTCGGCCCTT CTTACTTTGT GGAATACTTA ATTAAAGAAT CACCATGTAC TAAATCCCAG 660
GCCAGCAGCT GTTCACTTCA GTCCTCCGAC TCTGTGCCTG TTGGTCTTTG CAAAGGTTCT 720
CTGACTCGAA CACACTGGGA AAAGTTTGTC TCTGTGACTT GTGACTTCTT TGAATCACAG 780
GCTCCAGCCA CTGGAAGTGA AAACTCTGCT GTTAACCAGA AACCTACAAA CCTTCCCAAG 840
GTGGAAGAAT CCCAGCAGAA AAACACCCCC CCAACAGACT CCCCCTCCAA AGCTGGGCCA 900
AGAGGATCTG TCCAATATCT TCCTGACTTG GATGATAAAA ATTCCCAGGA AAAGGGCCCT 960
CAGGAGGCCT TTCCTGTGCA TCTGGACCTA ACCACGAATC CCCAGGGAGA AACCCTGGAT 1020
ATTTCCTTCC TCTTCCTGGA GCCTATGGAG GAGAAGCTGG TTGTCCTGCC TTTCCCCAAA 1080
GAAAAAGCAC GCACTGCTGA GTGCCCAGGG CCAGCCCAGA ATGCCAGCCC TCTTGTCCTT 1140
CCGCCA 1146

(2) INFORMATION FOR SEQ ID NO: 20:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 951

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Liver

(D) CLONE NAME: HP01299

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

ATGTGGCTCT ACCTGGCGGC CTTCGTGGGC CTGTACTACC TTCTGCACTG GTACCGGGAG 60
AGGCAGGTGG TGAGCCACCT CCAAGACAAG TATGTCTTTA TCACGGGCTG TGACTCGGGC 120
TTTGGGAACC TGCTGGCCAG ACAGCTGGAT GCACGAGGCT TGAGAGTGCT GGCTGCGTGT 180
CTGACGGAGA AGGGGGCCGA GCAGCTGAGG GGCCAGACGT CTGACAGGCT GGAGACGGTG 240

ACCCTGGATG TTACCAAGAT GGAGAGCATC GCTGCAGCTA CTCAGTGGGT GAAGGAGCAT 300
GTGGGGGACA GAGGACTCTG GGGACTGGTG AACAATGCAG GCATTCTTAC ACCAATTACC 360
TTATGTGAGT GGCTGAACAC TGAGGACTCT ATGAATATGC TCAAAGTGAA CCTCATTGGT 420
GTGATCCAGG TGACCTTGAG CATGCTTCCT TTGGTGAGGA GAGCACGGGG AAGAATTGTC 480
AATGTCTCCA GCATTCTGGG AAGAGTTGCT TTCTTTGTAG GAGGCTACTG TGTCTCCAAG 540
TATGGAGTGG AAGCCTTTTC AGATATTCTG AGGCGTGAGA TTCAACATTT TGGGGTGAAA 600
ATCAGCATAG TTGAACCTGG CTACTTCAGA ACGGGAATGA CAAACATGAC ACAGTCCTTA 660
GAGCGAATGA AGCAAAGTTG GAAAGAAGCC CCCAAGCATA TTAAGGAGAC CTATGGACAG 720
CAGTATTTTG ATGCCCTTTA CAATATCATG AAGGAAGGGC TGTTGAATTG TAGCACAAAC 780
CTGAACCTGG TCACTGACTG CATGGAACAT GCTCTGACAT CGGTGCATCC GCGAACTCGA 840
TATTCAGCTG GCTGGGATGC TAAATTTTTC TTCATCCCTC TATCTTATTT ACCTACATCA 900
CTGGCAGACT ACATTTTGAC TAGATCTTGG CCCAAACCAG CCCAGGCAGT C 951

(2) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 888

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Liver

(D) CLONE NAME: HP01347

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

ATGAGTGACT CCAAGGAACC AAGGGTGCAG CAGCTGGGCC TCCTGGGGTG TCTTGGCCAT 60
GGCGCCCTGG TGCTGCAACT CCTCTCCTTC ATGCTCTTGG CTGGGGTCCT GGTGGCCATC 120
CTTGTCCAAG TGTCCAAGGT CCCCAGCTCC CTAAGTCAGG AACAATCCGA GCAAGACGCA 180
ATCTACCAGA ACCTGACCCA GCTTAAAGCT GCAGTGGGTG AGCTCTCAGA GAAATCCAAG 240
CTGCAGGAGA TCTACCAGGA GCTGACCCAG CTGAAGGCTG CAGTGGGTGA GTTGCCAGAG 300
AAATCCAAGC TGCAGGAGAT CTACCAGGAG CTGACCCGGC TGAAGGCTGC AGTGGGTGAG 360
TTGCCAGAGA AATCCAAGCT GCAGGAGATC TACCAGGAGC TGACCCGGCT GAAGGCTGCA 420
GTGGGTGAGT TGCCAGAGAA ATCCAAGCTG CAGGAGATCT ACCAGGAGCT GACCCGGCTG 480
AAGGCTGCAG TGGGTGAGTT GCCAGAGAAA TCCAAGCTGC AGGAGATCTA CCAGGAGCTG 540

ACGGAGCTGA AGGCTGCAGT GGGTGAGTTG CCAGAGAAAT CCAAGCTGCA GGAGATCTAC 600
CAGGAGCTGA CCCAGCTGAA GGCTGCAGTG GGTGAGTTGC CAGACCAGTC CAAGCAGCAG 660
CAAATCTATC AAGAACTGAC CGATTTGAAG ACTGCATTTG AACGCCTGTG CCGCCACTGT 720
CCCAAGGACT GGACATTCTT CCAAGGAAAC TGTTACTTCA TGTCTAACTC CCAGCGGAAC 780
TGGCACGACT CCGTCACCGC CTGCCAGGAA GTGAGGGCCC AGCTCGTCGT AATCAAAACT 840
GCTGAGGAGC AGCTTCCAGC GGTACTGGAA CAGTGGAGAA CCCAACAA 888

(2) INFORMATION FOR SEQ ID NO: 22:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 591

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP01440

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

ATGTGTACGG GAAAATGTGC CCGCTGTGTG GGGCTCTCCC TCATTACCCT CTGCCTCGTC 60
TGCATTGTGG CCAACGCCCT CCTGCTGGTA CCTAATGGGG AGACCTCCTG GACCAACACC 120
AACCATCTCA GCTTGCAAGT CTGGCTCATG GGCGGCTTCA TTGGCGGGGG CCTAATGGTA 180
CTGTGTCCGG GGATTGCAGC CGTTCGGGCA GGGGGCAAGG GCTGCTGTGG TGCTGGGTGC 240
TGTGGAAACC GCTGCAGGAT GCTGCGCTCG GTCTTCTCCT CGGCGTTCGG GGTGCTTGGT 300
GCCATCTACT GCCTCTCGGT GTCTGGAGCT GGGCTCCGAA ATGGACCCAG ATGCTTAATG 360
AACGGCGAGT GGGGCTACCA CTTCGAAGAC ACCGCGGGAG CTTACTTGCT CAACCGCACT 420
CTATGGGATC GGTGCGAGGC GCCCCCTCGC GTGGTCCCCT GGAATGTGAC GCTCTTCTCG 480
CTGCTGGTGG CCGCCTCCTG CCTGGAGATA GTACTGTGTG GGATCCAGCT GGTGAACGCG 540
ACCATTGGTG TCTTCTGCGG CGATTGCAGG AAAAAACAGG ACACCCCTCA C 591

(2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 663

(B) TYPE: Nucleic acid
(C) STRANDEDNESS: Double
(D) TOPOLOGY: Linear
(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:
(A) ORGANISM: *Homo sapiens*
(B) CELL KIND: Stomach cancer
(D) CLONE NAME: HP01526

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:

```
ATGGAGGCGG GCGGCTTTCT GGACTCGCTC ATTTACGGAG CATGCGTGGT CTTCACCCTT     60
GGCATGTTCT CCGCCGGCCT CTCGGACCTC AGGCACATGC GAATGACCCG GAGTGTGGAC    120
AACGTCCAGT TCCTGCCCTT TCTCACCACG GAAGTCAACA ACCTGGGCTG GCTGAGTTAT    180
GGGGCTTTGA AGGGAGACGG GATCCTCATC GTCGTCAACA CAGTGGGTGC TGCGCTTCAG    240
ACCCTGTATA TCTTGGCATA TCTGCATTAC TGCCCTCGGA AGCGTGTTGT GCTCCTACAG    300
ACTGCAACCC TGCTAGGGGT CCTTCTCCTG GGTTATGGCT ACTTTTGGCT CCTGGTACCC    360
AACCCTGAGG CCCGGCTTCA GCAGTTGGGC CTCTTCTGCA GTGTCTTCAC CATCAGCATG    420
TACCTCTCAC CACTGGCTGA CTTGGCTAAG GTGATTCAAA CTAAATCAAC CCAATGTCTC    480
TCCTACCCAC TCACCATTGC TACCCTTCTC ACCTCTGCCT CCTGGTGCCT CTATGGGTTT    540
CGACTCAGAG ATCCCTATAT CATGGTGTCC AACTTTCCAG GAATCGTCAC CAGCTTTATC    600
CGCTTCTGGC TTTTCTGGAA GTACCCCCAG GAGCAAGACA GGAACTACTG GCTCCTGCAA    660
ACC                                                                  663
```

(2) INFORMATION FOR SEQ ID NO: 24:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 753
(B) TYPE: Nucleic acid
(C) STRANDEDNESS: Double
(D) TOPOLOGY: Linear
(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:
(A) ORGANISM: *Homo sapiens*
(B) CELL KIND: Stomach cancer
(D) CLONE NAME: HP10230

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

```
ATGTCGGACA TCGGAGACTG GTTCAGGAGC ATCCCGGCGA TCACGCGCTA TTGGTTCGCC    60
GCCACCGTCG CCGTGCCCTT GGTCGGCAAA CTCGGCCTCA TCAGCCCGGC CTACCTCTTC   120
CTCTGGCCCG AAGCCTTCCT TTATCGCTTT CAGATTTGGA GGCCAATCAC TGCCACCTTT   180
TATTTCCCTG TGGGTCCAGG AACTGGATTT CTTTATTTGG TCAATTTATA TTTCTTATAT   240
CAGTATTCTA CGCGACTTGA AACAGGAGCT TTTGATGGGA GGCCAGCAGA CTATTTATTC   300
ATGCTCCTCT TTAACTGGAT TTGCATCGTG ATTACTGGCT TAGCAATGGA TATGCAGTTG   360
CTGATGATTC CTCTGATCAT GTCAGTACTT TATGTCTGGG CCCAGCTGAA CAGAGACATG   420
ATTGTATCAT TTTGGTTTGG AACACGATTT AAGGCCTGCT ATTTACCCTG GGTTATCCTT   480
GGATTCAACT ATATCATCGG AGGCTCGGTA ATCAATGAGC TTATTGGAAA TCTGGTTGGA   540
CATCTTTATT TTTTCCTAAT GTTCAGATAC CCAATGGACT TGGGAGGAAG AAATTTTCTA   600
TCCACACCTC AGTTTTTGTA CCGCTGGCTG CCCAGTAGGA GAGGAGGAGT ATCAGGATTT   660
GGTGTGCCCC CTGCTAGCAT GAGGCGAGCT GCTGATCAGA ATGGCGGAGG CGGGAGACAC   720
AACTGGGGCC AGGGCTTTCG ACTTGGAGAC CAG                                753
```

(2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 318

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Epidermoid carcinoma

(C) CELL LINE: KB

(D) CLONE NAME: HP10389

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

```
ATGGCGACTC CCGGCCCTGT GATTCCGGAG GTCCCCTTTG AACCATCGAA GCCTCCAGTC    60
ATTGAGGGGC TGAGCCCCAC TGTTTACAGG AATCCAGAGA GTTTCAAGGA AAAGTTCGTT   120
CGCAAGACCC GCGAGAACCC GGTGGTACCC ATAGGTTGCC TGGCCACGGC GGCCGCCCTC   180
ACCTACGGCC TCTACTCCTT CCACCGGGGC AACAGCCAGC GCTCTCAGCT CATGATGCGC   240
ACCCGGATCG CCGCCCAGGG TTTCACGGTC GCAGCCATCT TGCTGGGTCT GGCTGTCACT   300
```

GCTATGAAGT CTCGACCC 318

(2) INFORMATION FOR SEQ ID NO: 26:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 234

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10408

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

ATGGGGTCTG GGCTGCCCCT TGTCCTCCTC TTGACCCTCC TTGGCAGCTC ACATGGAACA 60

GGGCCGGGTA TGACTTTGCA ACTGAAGCTG AAGGAGTCTT TTCTGACAAA TTCCTCCTAT 120

GAGTCCAGCT TCCTGGAATT GCTTGAAAAG CTCTGCCTCC TCCTCCATCT CCCTTCAGGG 180

ACCAGCGTCA CCCTCCACCA TGCAAGATCT CAACACCATG TTGTCTGCAA CACA 234

(2) INFORMATION FOR SEQ ID NO: 27:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 942

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10412

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

ATGGTGGCGC CTGTGTGGTA CTTGGTAGCG GCGGCTCTGC TAGTCGGCTT TATCCTCTTC 60
CTGACTCGCA GCCGGGGCCG GGCGGCATCA GCCGGCCAAG AGCCACTGCA CAATGAGGAG 120
CTGGCAGGAG CAGGCCGGGT GGCCCAGCCT GGGCCCCTGG AGCCTGAGGA GCCGAGAGCT 180
GGAGGCAGGC CTCGGCGCCG GAGGGACCTG GGCAGCCGCC TACAGGCCCA GCGTCGAGCC 240
CAGCGGGTGG CCTGGGCAGA AGCAGATGAG AACGAGGAGG AAGCTGTCAT CCTAGCCCAG 300
GAGGAGGAAG GTGTCGAGAA GCCAGCGGAA ACTCACCTGT CGGGGAAAAT TGGAGCTAAG 360
AAACTGCGGA AGCTGGAGGA GAAACAAGCG CGAAAGGCCC AGCGTGAGGC AGAGGAGGCT 420
GAACGTGAGG AGCGGAAACG ACTCGAGTCC CAGCGCGAAG CTGAGTGGAA GAAGGAGGAG 480
GAGCGGCTTC GCCTGGAGGA GGAGCAGAAG GAGGAGGAGG AGAGGAAGGC CCGCGAGGAG 540
CAGGCCCAGC GGGAGCATGA GGAGTACCTG AAACTGAAGG AGGCCTTTGT GGTGGAGGAG 600
GAAGGCGTAG GAGAGACCAT GACTGAGGAA CAGTCCCAGA GCTTCCTGAC AGAGTTCATC 660
AACTACATCA AGCAGTCCAA GGTTGTGCTC TTGGAAGACC TGGCTTCCCA GGTGGGCCTA 720
CGCACTCAGG ACACCATAAA TCGCATCCAG GACCTGCTGG CTGAGGGGAC TATAACAGGT 780
GTGATTGACG ACCGGGGCAA GTTCATCTAC ATAACCCCAG AGGAACTGGC CGCCGTGGCC 840
AACTTCATCC GACAGCGGGG CCGGGTGTCC ATCGCCGAGC TTGCCCAAGC CAGCAACTCC 900
CTCATCGCCT GGGGCCGGGA GTCCCCTGCC CAAGCCCCAG CC 942

(2) INFORMATION FOR SEQ ID NO: 28:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 585

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10413

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

ATGGCTGCCG AGGATGTGGT GGCGACTGGC GCCGACCCAA GCGATCTGGA GAGCGGCGGG 60
CTGCTGCATG AGATTTTCAC GTCGCCGCTC AACCTGCTGC TGCTTGGCCT CTGCATCTTC 120
CTGCTCTACA AGATCGTGCG CGGGGACCAG CCGGCGGCCA GCGGCGACAG CGACGACGAC 180
GAGCCGCCCC CTCTGCCCCG CCTCAAGCGG CGCGACTTCA CCCCCGCCGA GCTGCGGCGC 240
TTCGACGGCG TCCAGGACCC GCGCATACTC ATGGCCATCA ACGGCAAGGT GTTCGATGTG 300

ACCAAAGGCC GCAAATTCTA CGGGCCCGAG GGGCCGTATG GGTCTTTGC TGGAAGAGAT 360
GCATCCAGGG GCCTTGCCAC ATTTTGCCTG GATAAGGAAG CACTGAAGGA TGAGTACGAT 420
GACCTTTCTG ACCTCACTGC TGCCCAGCAG GAGACTCTGA GTGACTGGGA GTCTCAGTTC 480
ACTTTCAAGT ATCATCACGT GGGCAAACTG CTGAAGGAGG GGGAGGAGCC CACTGTGTAC 540
TCAGATGAGG AAGAACCAAA AGATGAGAGT GCCCGGAAAA ATGAT 585

(2) INFORMATION FOR SEQ ID NO: 29:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1386

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10415

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

ATGTTGGACT TCGCGATCTT CGCCGTTACC TTCTTGCTGG CGTTGGTGGG AGCCGTGCTC 60
TACCTCTATC CGGCTTCCAG ACAAGCTGCA GGAATTCCAG GGATTACTCC AACTGAAGAA 120
AAAGATGGTA ATCTTCCAGA TATTGTGAAT AGTGGAAGTT TGCATGAGTT CCTGGTTAAT 180
TTGCATGAGA GATATGGGCC TGTGGTCTCC TTCTGGTTTG GCAGGCGCCT CGTGGTTAGT 240
TTGGGCACTG TTGATGTACT GAAGCAGCAT ATCAATCCCA ATAAGACATT GGACCCTTTT 300
GAAACCATGC TGAAGTCATT ATTAAGGTAT CAATCTGGTG GTGGCAGTGT GAGTGAAAAC 360
CACATGAGGA AAAAATTGTA TGAAAATGGT GTGACTGATT CTCTGAAGAG TAACTTTGCC 420
CTCCTCCTAA AGCTTTCAGA AGAATTATTA GATAAATGGC TCTCCTACCC AGAGACCCAG 480
CACGTGCCCC TCAGCCAGCA TATGCTTGGT TTTGCTATGA AGTCTGTTAC ACAGATGGTA 540
ATGGGTAGTA CATTTGAAGA TGATCAGGAA GTCATTCGCT TCCAGAAGAA TCATGGCACA 600
GTTTGGTCTG AGATTGGAAA AGGCTTTCTA GATGGGTCAC TTGATAAAAA CATGACTCGG 660
AAAAAACAAT ATGAAGATGC CCTCATGCAA CTGGAGTCTG TTTTAAGGAA CATCATAAAA 720
GAACGAAAAG GAAGGAACTT CAGTCAACAT ATTTTCATTG ACTCCTTAGT ACAAGGGAAC 780
CTTAATGACC AACAGATCCT AGAAGACAGT ATGATATTTT CTCTGGCCAG TTGCATAATA 840
ACTGCAAAAT TGTGTACCTG GGCAATCTGT TTTTTAACCA CCTCTGAAGA AGTTCAAAAA 900
AAATTATATG AAGAGATAAA CCAAGTTTTT GGAAATGGTC CTGTTACTCC AGAGAAAATT 960

GAGCAGCTCA GATATTGTCA GCATGTGCTT TGTGAAACTG TTCGAACTGC CAAACTGACT 1020
CCAGTTTCTG CCCAGCTTCA AGATATTGAA GGAAAAATTG ACCGATTTAT TATTCCTAGA 1080
GAGACCCTCG TCCTTTATGC CCTTGGTGTG GTACTTCAGG ATCCTAATAC TTGGCCATCT 1140
CCACACAAGT TTGATCCAGA TCGGTTTGAT GATGAATTAG TAATGAAAAC TTTTTCCTCA 1200
CTTGGATTCT CAGGCACACA GGAGTGTCCA GAGTTGAGGT TTGCATATAT GGTGACCACA 1260
GTACTTCTTA GTGTATTGGT GAAGAGACTG CACCTACTTT CTGTGGAGGG ACAGGTTATT 1320
GAAACAAAGT ATGAACTGGT AACATCATCA AGGGAAGAAG CTTGGATCAC TGTCTCAAAG 1380
AGATAT 1386

(2) INFORMATION FOR SEQ ID NO: 30:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 741

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10419

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

ATGGGGGCTG CGGTGTTTTT CGGCTGCACT TTCGTCGCGT TCGGCCCGGC CTTCGCGCTT 60
TTCTTGATCA CTGTGGCTGG GGACCCGCTT CGCGTTATCA TCCTGGTCGC AGGGGCATTT 120
TTCTGGCTGG TCTCCCTGCT CCTGGCCTCT GTGGTCTGGT TCATCTTGGT CCATGTGACC 180
GACCGGTCAG ATGCCCGGCT CCAGTACGGC CTCCTGATTT TTGGTGCTGC TGTCTCTGTC 240
CTTCTACAGG AGGTGTTCCG CTTTGCCTAC TACAAGCTGC TTAAGAAGGC AGATGAGGGG 300
TTAGCATCGC TGAGTGAGGA CGGAAGATCA CCCATCTCCA TCCGCCAGAT GGCCTATGTT 360
TCTGGTCTCT CCTTCGGTAT CATCAGTGGT GTCTTCTCTG TTATCAATAT TTTGGCTGAT 420
GCACTTGGGC CAGGTGTGGT TGGGATCCAT GGAGACTCAC CCTATTACTT CCTGACTTCA 480
GCCTTTCTGA CAGCAGCCAT TATCCTGCTC CATACCTTTT GGGGAGTTGT GTTCTTTGAT 540
GCCTGTGAGA GGAGACGGTA CTGGGCTTTG GGCCTGGTGG TTGGGAGTCA CCTACTGACA 600
TCGGGACTGA CATTCCTGAA CCCCTGGTAT GAGGCCAGCC TGCTGCCCAT CTATGCAGTC 660
ACTGTTTCCA TGGGGCTCTG GGCCTTCATC ACAGCTGGAG GGTCCCTCCG AAGTATTCAG 720
CGCAGCCTCT TGTGTAAGGA C 741

(2) INFORMATION FOR SEQ ID NO: 31:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 339

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10424

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

```
ATGAACTTCT ATTTACTCCT AGCGAGCAGC ATTCTGTGTG CCTTGATTGT CTTCTGGAAA     60
TATCGCCGCT TTCAGAGAAA CACTGGCGAA ATGTCATCAA ATTCAACTGC TCTTGCACTA    120
GTGAGACCCT CTTCTTCTGG GTTAATTAAC AGCAATACAG ACAACAATCT TGCAGTCTAC    180
GACCTCTCTC GGGATATTTT AAATAATTTC CCACACTCAA TAGCCAGGCA GAAGCGAATA    240
TTGGTAAACC TCAGTATGGT GGAAAACAAG CTGGTTGAAC TGGAACATAC TCTACTTAGC    300
AAGGGTTTCA GAGGTGCATC ACCTCACCGG AAATCCACC                           339
```

(2) INFORMATION FOR SEQ ID NO: 32:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1095

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Epidermoid carcinoma

(C) CELL LINE: KB

(D) CLONE NAME: HP10428

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

ATGGGGAGGT GGGCCCTCGA TGTGGCCTTT TTGTGGAAGG CGGTGTTGAC CCTGGGGCTG 60
GTGCTTCTCT ACTACTGCTT CTCCATCGGC ATCACCTTCT ACAACAAGTG GCTGACAAAG 120
AGCTTCCATT TCCCCCTCTT CATGACGATG CTGCACCTGG CCGTGATCTT CCTCTTCTCC 180
GCCCTGTCCA GGGCGCTGGT TCAGTGCTCC AGCCACAGGG CCCGTGTGGT GCTGAGCTGG 240
GCCGACTACC TCAGAAGAGT GGCTCCCACA GCTCTGGCGA CGGCGCTTGA CGTGGGCTTG 300
TCCAACTGGA GCTTCCTGTA TGTCACCGTC TCGCTGTACA CAATGACCAA ATCCTCAGCT 360
GTCCTCTTCA TCTTGATCTT CTCTCTGATC TTCAAGCTGG AGGAGCTGCG CGCGGCACTG 420
GTCCTGGTGG TCCTCCTCAT CGCCGGGGGT CTCTTCATGT TCACCTACAA GTCCACACAG 480
TTCAACGTGG AGGGCTTCGC CTTGGTGCTG GGGGCCTCGT TCATCGGTGG CATTCGCTGG 540
ACCCTCACCC AGATGCTCCT GCAGAAGGCT GAACTCGGCC TCCAGAATCC CATCGACACC 600
ATGTTCCACC TGCAGCCACT CATGTTCCTG GGGCTCTTCC CTCTCTTTGC TGTATTTGAA 660
GGTCTCCATT TGTCCACATC TGAGAAAATC TTCCGTTTCC AGGACACAGG GCTGCTCCTG 720
CGGGTACTTG GGAGCCTCTT CCTTGGCGGG ATTCTCGCCT TTGGTTTGGG CTTCTCTGAG 780
TTCCTCCTGG TCTCCAGAAC CTCCAGCCTC ACTCTCTCCA TTGCCGGCAT TTTTAAGGAA 840
GTCTGCACTT TGCTGTTGGC AGCTCATCTG CTGGGCGATC AGATCAGCCT CCTGAACTGG 900
CTGGGCTTCG CCCTCTGCCT CTCGGGAATA TCCCTCCACG TTGCCCTCAA AGCCCTGCAT 960
TCCAGAGGTG ATGGTGGCCC CAAGGCCTTG AAGGGGCTGG GCTCCAGCCC CGACCTGGAG 1020
CTGCTGCTCC GGAGCAGCCA GCGGGAGGAA GGTGACAATG AGGAGGAGGA GTACTTTGTG 1080
GCCCAGGGGC AGCAG 1095

(2) INFORMATION FOR SEQ ID NO: 33:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 678

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10429

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

ATGCCTACCA CAAAGAAGAC ATTGATGTTC TTATCAAGCT TTTTCACCAG CCTTGGGTCC 60
TTCATTGTAA TTTGCTCTAT TCTTGGGACA CAAGCATGGA TCACCAGTAC AATTGCTGTT 120
AGAGACTCTG CTTCAAATGG GAGCATTTTC ATCACTTACG GACTTTTTCG TGGGGAGAGT 180
AGTGAAGAAT TGAGTCACGG ACTTGCAGAA CCAAAGAAAA AGTTTGCAGT TTTAGAGATA 240
CTGAATAATT CTTCCCAAAA AACTCTGCAT TCGGTGACTA TCCTGTTCCT GGTCCTGAGT 300
TTGATCACGT CGCTGCTGAG CTCTGGGTTT ACCTTCTACA ACAGCATCAG CAACCCTTAC 360
CAGACATTCC TGGGGCCGAC GGGGGTGTAC ACCTGGAACG GGCTCGGTGC ATCCTTCGTT 420
TTTGTGACCA TGATACTGTT TGTGGCGAAC ACGCAGTCCA ACCAACTCTC CGAAGAGTTG 480
TTCCAAATGC TTTACCCGGC AACCACCAGT AAAGGAACGA CCCACAGTTA CGGATACTCG 540
TTCTGGCTCA TACTGCTCGT CATTCTTCTA AATATAGTCA CTGTAACCAT CATCATTTTC 600
TACCAGAAGG CCAGATACCA GCGGAAGCAG GAGCAGAGAA AGCCAATGGA ATATGCTCCA 660
AGGGACGGAA TTTTATTC 678

(2) INFORMATION FOR SEQ ID NO: 34:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 387

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Liver

(D) CLONE NAME: HP10432

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

ATGGCTCGGG GCTCGCTGCG CCGGTTGCTG CGGCTCCTCG TGCTGGGGCT CTGGCTGGCG 60
TTGCTGCGCT CCGTGGCCGG GGAGCAAGCG CCAGGCACCG CCCCCTGCTC CCGCGGCAGC 120
TCCTGGAGCG CGGACCTGGA CAAGTGCATG GACTGCGCGT CTTGCAGGGC GCGACCGCAC 180
AGCGACTTCT GCCTGGGCTG CGCTGCAGCA CCTCCTGCCC CCTTCCGGCT GCTTTGGCCC 240
ATCCTTGGGG GCGCTCTGAG CCTGACCTTC GTGCTGGGGC TGCTTTCTGG CTTTTGGTC 300
TGGAGACGAT GCCGCAGGAG AGAGAAGTTC ACCACCCCCA TAGAGGAGAC CGGCGGAGAG 360
GGCTGCCCAG CTGTGGCGCT GATCCAG 387

(2) INFORMATION FOR SEQ ID NO: 35:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 489

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Liver

(D) CLONE NAME: HP10433

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

```
ATGCGACGGC TGCTGATCCC TCTGGCCCTG TGGCTGGGCG CGGTGGGCGT GGGCGTCGCC    60
GAGCTCACGG AAGCCCAGCG CCGGGGCCTG CAGGTGGCCC TGGAGGAATT TCACAAGCAC   120
CCGCCCGTGC AGTGGGCCTT CCAGGAGACC AGTGTGGAGA GCGCCGTGGA CACGCCCTTC   180
CCAGCTGGAA TATTTGTGAG GCTGGAATTT AAGCTGCAGC AGACAAGCTG CCGGAAGAGG   240
GACTGGAAGA AACCCGAGTG CAAAGTCAGG CCCAATGGGA GGAAACGGAA ATGCCTGGCC   300
TGCATCAAAC TGGGCTCTGA GGACAAAGTT CTGGGCCGGT TGGTCCACTG CCCCATAGAG   360
ACCCAAGTTC TGCGGGAGGC TGAGGAGCAC CAGGAGACCC AGTGCCTCAG GGTGCAGCGG   420
GCTGGTGAGG ACCCCCACAG CTTCTACTTC CCTGGACAGT TCGCCTTCTC CAAGGCCCTG   480
CCCCGCAGC                                                           489
```

(2) INFORMATION FOR SEQ ID NO: 36:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 579

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10480

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

```
ATGATCCGCT GCGGCCTGGC CTGCGAGCGC TGCCGCTGGA TCCTGCCCCT GCTCCTACTC     60
AGCGCCATCG CCTTCGACAT CATCGCGCTG GCCGGCCGCG GCTGGTTGCA GTCTAGCGAC    120
CACGGCCAGA CGTCCTCGCT GTGGTGGAAA TGCTCCCAAG AGGGCGGCGG CAGCGGGTCC    180
TACGAGGAGG GCTGTCAGAG CCTCATGGAG TACGCGTGGG GTAGAGCAGC GGCTGCCATG    240
CTCTTCTGTG GCTTCATCAT CCTGGTGATC TGTTTCATCC TCTCCTTCTT CGCCCTCTGT    300
GGACCCCAGA TGCTTGTCTT CCTGAGAGTG ATTGGAGGTC TCCTTGCCTT GGCTGCTGTG    360
TTCCAGATCA TCTCCCTGGT AATTTACCCC GTGAAGTACA CCCAGACCTT CACCCTTCAT    420
GCCAACCGTG CTGTCACTTA CATCTATAAC TGGGCCTACG GCTTTGGGTG GGCAGCCACG    480
ATTATCCTGA TCGGCTGTGC CTTCTTCTTC TGCTGCCTCC CCAACTACGA AGATGACCTT    540
CTGGGCAATG CCAAGCCCAG GTACTTCTAC ACATCTGCC                           579
```

(2) INFORMATION FOR SEQ ID NO: 37:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1502

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Liver

(D) CLONE NAME: HP01263

(ix) SEQUENCE CHARACTERISTICS:

(A) CHARACTERIZATION CODE: CDS

(B) EXISTENCE POSITION: 37.. 1185

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:

```
ACAAACTGAC CCATCCTGGG CCTTGTTCTC CACAGA ATG GGT CTG CTC CTT CCC      54
                                        Met Gly Leu Leu Leu Pro
                                          1               5
CTG GCA CTC TGC ATC CTA GTC CTG TGC TGC GGA GCA ATG TCT CCA CCC      102
```

Leu Ala Leu Cys Ile Leu Val Leu Cys Cys Gly Ala Met Ser Pro Pro
10 15 20
CAG CTG GCC CTC AAC CCC TCG GCT CTG CTC TCC CGG GGC TGC AAT GAC 150
Gln Leu Ala Leu Asn Pro Ser Ala Leu Leu Ser Arg Gly Cys Asn Asp
25 30 35
TCC GAT GTG CTG GCA GTT GCA GGC TTT GCC CTG CGG GAT ATT AAC AAA 198
Ser Asp Val Leu Ala Val Ala Gly Phe Ala Leu Arg Asp Ile Asn Lys
40 45 50
GAC AGA AAG GAT GGC TAT GTG CTG AGA CTC AAC CGA GTG AAC GAC GCC 246
Asp Arg Lys Asp Gly Tyr Val Leu Arg Leu Asn Arg Val Asn Asp Ala
55 60 65 70
CAG GAA TAC AGA CGG GGT GGC CTG GGA TCT CTG TTC TAT CTT ACA CTG 294
Gln Glu Tyr Arg Arg Gly Gly Leu Gly Ser Leu Phe Tyr Leu Thr Leu
75 80 85
GAT GTG CTA GAG ACT GAC TGC CAT GTG CTC AGA AAG AAG GCA TGG CAA 342
Asp Val Leu Glu Thr Asp Cys His Val Leu Arg Lys Lys Ala Trp Gln
90 95 100
GAC TGT GGA ATG AGG ATA TTT TTT GAA TCA GTT TAT GGT CAA TGC AAA 390
Asp Cys Gly Met Arg Ile Phe Phe Glu Ser Val Tyr Gly Gln Cys Lys
105 110 115
GCA ATA TTT TAT ATG AAC AAC CCA AGT AGA GTT CTC TAT TTA GCT GCT 438
Ala Ile Phe Tyr Met Asn Asn Pro Ser Arg Val Leu Tyr Leu Ala Ala
120 125 130
TAT AAC TGT ACT CTT CGC CCA GTT TCA AAA AAA AAG ATT TAC ATG ACG 486
Tyr Asn Cys Thr Leu Arg Pro Val Ser Lys Lys Lys Ile Tyr Met Thr
135 140 145 150
TGC CCT GAC TGC CCA AGC TCC ATA CCC ACT GAC TCT TCC AAT CAC CAA 534
Cys Pro Asp Cys Pro Ser Ser Ile Pro Thr Asp Ser Ser Asn His Gln
155 160 165
GTG CTG GAG GCT GCC ACC GAG TCT CTT GCG AAA TAC AAC AAT GAG AAC 582
Val Leu Glu Ala Ala Thr Glu Ser Leu Ala Lys Tyr Asn Asn Glu Asn
170 175 180
ACA TCC AAG CAG TAT TCT CTC TTC AAA GTC ACC AGG GCT TCT AGC CAG 630
Thr Ser Lys Gln Tyr Ser Leu Phe Lys Val Thr Arg Ala Ser Ser Gln
185 190 195
TGG GTG GTC GGC CCT TCT TAC TTT GTG GAA TAC TTA ATT AAA GAA TCA 678
Trp Val Val Gly Pro Ser Tyr Phe Val Glu Tyr Leu Ile Lys Glu Ser
200 205 210

```
CCA TGT ACT AAA TCC CAG GCC AGC AGC TGT TCA CTT CAG TCC TCC GAC      726
Pro Cys Thr Lys Ser Gln Ala Ser Ser Cys Ser Leu Gln Ser Ser Asp
215                 220                 225                 230
TCT GTG CCT GTT GGT CTT TGC AAA GGT TCT CTG ACT CGA ACA CAC TGG      774
Ser Val Pro Val Gly Leu Cys Lys Gly Ser Leu Thr Arg Thr His Trp
                235                 240                 245
GAA AAG TTT GTC TCT GTG ACT TGT GAC TTC TTT GAA TCA CAG GCT CCA      822
Glu Lys Phe Val Ser Val Thr Cys Asp Phe Phe Glu Ser Gln Ala Pro
            250                 255                 260
GCC ACT GGA AGT GAA AAC TCT GCT GTT AAC CAG AAA CCT ACA AAC CTT      870
Ala Thr Gly Ser Glu Asn Ser Ala Val Asn Gln Lys Pro Thr Asn Leu
        265                 270                 275
CCC AAG GTG GAA GAA TCC CAG CAG AAA AAC ACC CCC CCA ACA GAC TCC      918
Pro Lys Val Glu Glu Ser Gln Gln Lys Asn Thr Pro Pro Thr Asp Ser
    280                 285                 290
CCC TCC AAA GCT GGG CCA AGA GGA TCT GTC CAA TAT CTT CCT GAC TTG      966
Pro Ser Lys Ala Gly Pro Arg Gly Ser Val Gln Tyr Leu Pro Asp Leu
295                 300                 305                 310
GAT GAT AAA AAT TCC CAG GAA AAG GGC CCT CAG GAG GCC TTT CCT GTG     1014
Asp Asp Lys Asn Ser Gln Glu Lys Gly Pro Gln Glu Ala Phe Pro Val
                315                 320                 325
CAT CTG GAC CTA ACC ACG AAT CCC CAG GGA GAA ACC CTG GAT ATT TCC     1062
His Leu Asp Leu Thr Thr Asn Pro Gln Gly Glu Thr Leu Asp Ile Ser
            330                 335                 340
TTC CTC TTC CTG GAG CCT ATG GAG GAG AAG CTG GTT GTC CTG CCT TTC     1110
Phe Leu Phe Leu Glu Pro Met Glu Glu Lys Leu Val Val Leu Pro Phe
        345                 350                 355
CCC AAA GAA AAA GCA CGC ACT GCT GAG TGC CCA GGG CCA GCC CAG AAT     1158
Pro Lys Glu Lys Ala Arg Thr Ala Glu Cys Pro Gly Pro Ala Gln Asn
    360                 365                 370
GCC AGC CCT CTT GTC CTT CCG CCA TGAGAATCAC ACAGAGTCTT CTGTAGGG      1210
Ala Ser Pro Leu Val Leu Pro Pro
375                 380
GTATGGTGCG CCGCATGACA TGGGAGGCGA TGGGGACGAT GGACAGAGAC AGAGCGTGCA   1270
CACGTAGAGT GGCTAGTGAA GGACGCCTTT TTGACTCTTC TTGGTCTCAG CATGTTGACT   1330
GGGATTGGAA ATAATGAGAC TGAGCCCTCG GCTTGGGCTG CACTCTACCC TGTACACTGC   1390
CTTGTACCCT GAGCTGCATC ACCTCCTAAA CTGAGCAGTC TCATACCATG GAGAGATGCC   1450
TCTCTTATGT CTTCAGCCAC TCACTTATAA AGATACTTAT CTTTTCAGCA GT           1502
```

(2) INFORMATION FOR SEQ ID NO: 38:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1349

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Liver

(D) CLONE NAME: HP01299

(ix) SEQUENCE CHARACTERISTICS:

(A) CHARACTERIZATION CODE: CDS

(B) EXISTENCE POSITION: 111.. 1064

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

```
AGCAGTTGGG GCAGGAGGAA GCCGACTGCT GCCTGGTCTG CAAAGAAGTC CTTTCAAGTC     60
TCTAGGACTG GACTCTTCCT AAGCAAGTCC GAGAAGGAAG CACCCTCACT ATG TGG        116
                                                          Met Trp
                                                            1
CTC TAC CTG GCG GCC TTC GTG GGC CTG TAC TAC CTT CTG CAC TGG TAC
164
Leu Tyr Leu Ala Ala Phe Val Gly Leu Tyr Tyr Leu Leu His Trp Tyr
          5                  10                  15
CGG GAG AGG CAG GTG GTG AGC CAC CTC CAA GAC AAG TAT GTC TTT ATC       212
Arg Glu Arg Gln Val Val Ser His Leu Gln Asp Lys Tyr Val Phe Ile
     20                  25                  30
ACG GGC TGT GAC TCG GGC TTT GGG AAC CTG CTG GCC AGA CAG CTG GAT       260
Thr Gly Cys Asp Ser Gly Phe Gly Asn Leu Leu Ala Arg Gln Leu Asp
 35                  40                  45                  50
GCA CGA GGC TTG AGA GTG CTG GCT GCG TGT CTG ACG GAG AAG GGG GCC       308
Ala Arg Gly Leu Arg Val Leu Ala Ala Cys Leu Thr Glu Lys Gly Ala
```

55 60 65

GAG CAG CTG AGG GGC CAG ACG TCT GAC AGG CTG GAG ACG GTG ACC CTG 356

Glu Gln Leu Arg Gly Gln Thr Ser Asp Arg Leu Glu Thr Val Thr Leu

70 75 80

GAT GTT ACC AAG ATG GAG AGC ATC GCT GCA GCT ACT CAG TGG GTG AAG 404

Asp Val Thr Lys Met Glu Ser Ile Ala Ala Ala Thr Gln Trp Val Lys

85 90 95

GAG CAT GTG GGG GAC AGA GGA CTC TGG GGA CTG GTG AAC AAT GCA GGC 452

Glu His Val Gly Asp Arg Gly Leu Trp Gly Leu Val Asn Asn Ala Gly

100 105 110

ATT CTT ACA CCA ATT ACC TTA TGT GAG TGG CTG AAC ACT GAG GAC TCT 500

Ile Leu Thr Pro Ile Thr Leu Cys Glu Trp Leu Asn Thr Glu Asp Ser

115 120 125 130

ATG AAT ATG CTC AAA GTG AAC CTC ATT GGT GTG ATC CAG GTG ACC TTG 548

Met Asn Met Leu Lys Val Asn Leu Ile Gly Val Ile Gln Val Thr Leu

135 140 145

AGC ATG CTT CCT TTG GTG AGG AGA GCA CGG GGA AGA ATT GTC AAT GTC 596

Ser Met Leu Pro Leu Val Arg Arg Ala Arg Gly Arg Ile Val Asn Val

150 155 160

TCC AGC ATT CTG GGA AGA GTT GCT TTC TTT GTA GGA GGC TAC TGT GTC 644

Ser Ser Ile Leu Gly Arg Val Ala Phe Phe Val Gly Gly Tyr Cys Val

165 170 175

TCC AAG TAT GGA GTG GAA GCC TTT TCA GAT ATT CTG AGG CGT GAG ATT 692

Ser Lys Tyr Gly Val Glu Ala Phe Ser Asp Ile Leu Arg Arg Glu Ile

180 185 190

CAA CAT TTT GGG GTG AAA ATC AGC ATA GTT GAA CCT GGC TAC TTC AGA 740

Gln His Phe Gly Val Lys Ile Ser Ile Val Glu Pro Gly Tyr Phe Arg

195 200 205 210

ACG GGA ATG ACA AAC ATG ACA CAG TCC TTA GAG CGA ATG AAG CAA AGT 788

Thr Gly Met Thr Asn Met Thr Gln Ser Leu Glu Arg Met Lys Gln Ser

215 220 225

TGG AAA GAA GCC CCC AAG CAT ATT AAG GAG ACC TAT GGA CAG CAG TAT 836

Trp Lys Glu Ala Pro Lys His Ile Lys Glu Thr Tyr Gly Gln Gln Tyr

230 235 240

TTT GAT GCC CTT TAC AAT ATC ATG AAG GAA GGG CTG TTG AAT TGT AGC 884

Phe Asp Ala Leu Tyr Asn Ile Met Lys Glu Gly Leu Leu Asn Cys Ser

245 250 255

ACA AAC CTG AAC CTG GTC ACT GAC TGC ATG GAA CAT GCT CTG ACA TCG 932

```
Thr Asn Leu Asn Leu Val Thr Asp Cys Met Glu His Ala Leu Thr Ser
    260                 265                 270
GTG CAT CCG CGA ACT CGA TAT TCA GCT GGC TGG GAT GCT AAA TTT TTC      980
Val His Pro Arg Thr Arg Tyr Ser Ala Gly Trp Asp Ala Lys Phe Phe
275                 280                 285                 290
TTC ATC CCT CTA TCT TAT TTA CCT ACA TCA CTG GCA GAC TAC ATT TTG     1028
Phe Ile Pro Leu Ser Tyr Leu Pro Thr Ser Leu Ala Asp Tyr Ile Leu
                295                 300                 305
ACT AGA TCT TGG CCC AAA CCA GCC CAG GCA GTC TAAAGAAAAC TGGGTTGGT    1080
Thr Arg Ser Trp Pro Lys Pro Ala Gln Ala Val
            310                 315
GCTTCTTGGA ATGAAGGCAA AAATCTGAAA TTGTTAGTGT CTCAGTAATC CTGATTTAGA   1140
ACCCAGGCTT TTTGTAACAA TGTGTTTTCT TGCCTAAATT CATTTATCTG GCATCATCAG   1200
AGTACTAACA TGTTTATATT TCAGATATCC AAAGCTTACC ACTTTAGGTG ATGAATCTTT   1260
ACTATTTTAG CCCTTTTTTG ATGAGACTAT TTGTCTAAAG TGAATCATTT GTTCTTGCCT   1320
TATTAAACAG AGTAGATGGA AAACAATTT                                     1349
```

(2) INFORMATION FOR SEQ ID NO: 39:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1643

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Liver

(D) CLONE NAME: HP01347

(ix) SEQUENCE CHARACTERISTICS:

(A) CHARACTERIZATION CODE: CDS

(B) EXISTENCE POSITION: 25.. 915

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

```
AACATCTGGG GACAGCGGGA AAAC ATG AGT GAC TCC AAG GAA CCA AGG GTG     51
                           Met Ser Asp Ser Lys Glu Pro Arg Val
                             1               5
CAG CAG CTG GGC CTC CTG GGG TGT CTT GGC CAT GGC GCC CTG GTG CTG    99
Gln Gln Leu Gly Leu Leu Gly Cys Leu Gly His Gly Ala Leu Val Leu
 10                  15                  20                  25
CAA CTC CTC TCC TTC ATG CTC TTG GCT GGG GTC CTG GTG GCC ATC CTT   147
Gln Leu Leu Ser Phe Met Leu Leu Ala Gly Val Leu Val Ala Ile Leu
                     30                  35                  40
GTC CAA GTG TCC AAG GTC CCC AGC TCC CTA AGT CAG GAA CAA TCC GAG   195
Val Gln Val Ser Lys Val Pro Ser Ser Leu Ser Gln Glu Gln Ser Glu
                 45                  50                  55
CAA GAC GCA ATC TAC CAG AAC CTG ACC CAG CTT AAA GCT GCA GTG GGT   243
Gln Asp Ala Ile Tyr Gln Asn Leu Thr Gln Leu Lys Ala Ala Val Gly
             60                  65                  70
GAG CTC TCA GAG AAA TCC AAG CTG CAG GAG ATC TAC CAG GAG CTG ACC   291
Glu Leu Ser Glu Lys Ser Lys Leu Gln Glu Ile Tyr Gln Glu Leu Thr
         75                  80                  85
CAG CTG AAG GCT GCA GTG GGT GAG TTG CCA GAG AAA TCC AAG CTG CAG   339
Gln Leu Lys Ala Ala Val Gly Glu Leu Pro Glu Lys Ser Lys Leu Gln
 90                  95                 100                 105
GAG ATC TAC CAG GAG CTG ACC CGG CTG AAG GCT GCA GTG GGT GAG TTG   387
Glu Ile Tyr Gln Glu Leu Thr Arg Leu Lys Ala-Ala Val Gly Glu Leu
                    110                 115                 120
CCA GAG AAA TCC AAG CTG CAG GAG ATC TAC CAG GAG CTG ACC CGG CTG   435
Pro Glu Lys Ser Lys Leu Gln Glu Ile Tyr Gln Glu Leu Thr Arg Leu
                125                 130                 135
AAG GCT GCA GTG GGT GAG TTG CCA GAG AAA TCC AAG CTG CAG GAG ATC   483
Lys Ala Ala Val Gly Glu Leu Pro Glu Lys Ser Lys Leu Gln Glu Ile
            140                 145                 150
TAC CAG GAG CTG ACC CGG CTG AAG GCT GCA GTG GGT GAG TTG CCA GAG   531
Tyr Gln Glu Leu Thr Arg Leu Lys Ala Ala Val Gly Glu Leu Pro Glu
        155                 160                 165
AAA TCC AAG CTG CAG GAG ATC TAC CAG GAG CTG ACG GAG CTG AAG GCT   579
Lys Ser Lys Leu Gln Glu Ile Tyr Gln Glu Leu Thr Glu Leu Lys Ala
170                 175                 180                 185
GCA GTG GGT GAG TTG CCA GAG AAA TCC AAG CTG CAG GAG ATC TAC CAG   627
Ala Val Gly Glu Leu Pro Glu Lys Ser Lys Leu Gln Glu Ile Tyr Gln
```

```
                    190                 195                 200
GAG CTG ACC CAG CTG AAG GCT GCA GTG GGT GAG TTG CCA GAC CAG TCC      675
Glu Leu Thr Gln Leu Lys Ala Ala Val Gly Glu Leu Pro Asp Gln Ser
            205                 210                 215
AAG CAG CAG CAA ATC TAT CAA GAA CTG ACC GAT TTG AAG ACT GCA TTT      723
Lys Gln Gln Gln Ile Tyr Gln Glu Leu Thr Asp Leu Lys Thr Ala Phe
        220                 225                 230
GAA CGC CTG TGC CGC CAC TGT CCC AAG GAC TGG ACA TTC TTC CAA GGA      771
Glu Arg Leu Cys Arg His Cys Pro Lys Asp Trp Thr Phe Phe Gln Gly
    235                 240                 245
AAC TGT TAC TTC ATG TCT AAC TCC CAG CGG AAC TGG CAC GAC TCC GTC      819
Asn Cys Tyr Phe Met Ser Asn Ser Gln Arg Asn Trp His Asp Ser Val
250                 255                 260                 265
ACC GCC TGC CAG GAA GTG AGG GCC CAG CTC GTC GTA ATC AAA ACT GCT      867
Thr Ala Cys Gln Glu Val Arg Ala Gln Leu Val Val Ile Lys Thr Ala
                270                 275                 280
GAG GAG CAG CTT CCA GCG GTA CTG GAA CAG TGG AGA ACC CAA CAA           912
Glu Glu Gln Leu Pro Ala Val Leu Glu Gln Trp Arg Thr Gln Gln
            285                 290                 295
TAGCGGGAAT GAAGACTGTG CGGAATTTAG TGGCAGTGGC TGGAACGACA ATCGATGT      970
GACGTTGACA ATTACTGGAT CTGCAAAAAG CCCGCAGCCT GCTTCAGAGA CGAATAGTTG   1030
TTTCCCTGCT AGCCTCAGCC TCCATTGTGG TATAGCAGAA CTTCACCCAC TTGTAAGCCA   1090
GCGCTTCTTC TCTCCATCCT TGGACCTTCA CAAATGCCCT GAGACGGTTC TCTGTTCGAT   1150
TTTTCATCCC CTATGAACCT GGGTCTTATT CTGTCCTTCT GATGCCTCCA AGTTTCCCTG   1210
GTGTAGAGCT TGTGTTCTTG GCCCATCCTT GGAGCTTTAT AAGTGACCTG AGTGGGATGC   1270
ATTTAGGGGG CGGGCTTGGT ATGTTGTATG AATCCACTCT CTGTTCCTTT TGGAGATTAG   1330
ACTATTTGGA TTCATGTGTA GCTGCCCTGT CCCCTGGGGC TTTATCTCAT CCATGCAAAC   1390
TACCATCTGC TCAACTTCCA GCTACACCCC GTGCACCCTT TTGACTGGGG ACTTGCTGGT   1450
TGAAGGAGCT CATCTTGCAG GCTGGAAGCA CCAGGGAATT AATTCCCCCA GTCAACCAAT   1510
GGCATCCAGA GAGGGCATGG AGGCTCCATA CAACCTCTTC CACCCCCACA TCTTTCTTTG   1570
TCCTATACAT GTCTTCCATT TGGCTGTTTC TGAGTTGTAG CCTTTATAAT AAAGTGGTAA   1630
ATGTTGTAAC TGC                                                      1643
```

(2) INFORMATION FOR SEQ ID NO: 40:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 729

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP01440

(ix) SEQUENCE CHARACTERISTICS:

(A) CHARACTERIZATION CODE: CDS

(B) EXISTENCE POSITION: 38.. 631

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

```
ACTTTCACTC ACCGCCTGTC CTTCCTGACA CCTCACC ATG TGT ACG GGA AAA TGT      55
                                          Met Cys Thr Gly Lys Cys
                                            1               5
GCC CGC TGT GTG GGG CTC TCC CTC ATT ACC CTC TGC CTC GTC TGC ATT      103
Ala Arg Cys Val Gly Leu Ser Leu Ile Thr Leu Cys Leu Val Cys Ile
          10                  15                  20
GTG GCC AAC GCC CTC CTG CTG GTA CCT AAT GGG GAG ACC TCC TGG ACC      151
Val Ala Asn Ala Leu Leu Leu Val Pro Asn Gly Glu Thr Ser Trp Thr
      25                  30                  35
AAC ACC AAC CAT CTC AGC TTG CAA GTC TGG CTC ATG GGC GGC TTC ATT      199
Asn Thr Asn His Leu Ser Leu Gln Val Trp Leu Met Gly Gly Phe Ile
  40                  45                  50
GGC GGG GGC CTA ATG GTA CTG TGT CCG GGG ATT GCA GCC GTT CGG GCA      247
Gly Gly Gly Leu Met Val Leu Cys Pro Gly Ile Ala Ala Val Arg Ala
55                  60                  65                  70
GGG GGC AAG GGC TGC TGT GGT GCT GGG TGC TGT GGA AAC CGC TGC AGG      295
Gly Gly Lys Gly Cys Cys Gly Ala Gly Cys Cys Gly Asn Arg Cys Arg
                  75                  80                  85
ATG CTG CGC TCG GTC TTC TCC TCG GCG TTC GGG GTG CTT GGT GCC ATC      343
Met Leu Arg Ser Val Phe Ser Ser Ala Phe Gly Val Leu Gly Ala Ile
              90                  95                  100
TAC TGC CTC TCG GTG TCT GGA GCT GGG CTC CGA AAT GGA CCC AGA TGC      391
```

Tyr Cys Leu Ser Val Ser Gly Ala Gly Leu Arg Asn Gly Pro Arg Cys
        105   110   115
TTA ATG AAC GGC GAG TGG GGC TAC CAC TTC GAA GAC ACC GCG GGA GCT   439
Leu Met Asn Gly Glu Trp Gly Tyr His Phe Glu Asp Thr Ala Gly Ala
    120   125   130
TAC TTG CTC AAC CGC ACT CTA TGG GAT CGG TGC GAG GCG CCC CCT CGC   487
Tyr Leu Leu Asn Arg Thr Leu Trp Asp Arg Cys Glu Ala Pro Pro Arg
135   140   145   150
GTG GTC CCC TGG AAT GTG ACG CTC TTC TCG CTG CTG GTG GCC GCC TCC   535
Val Val Pro Trp Asn Val Thr Leu Phe Ser Leu Leu Val Ala Ala Ser
                155   160   165
TGC CTG GAG ATA GTA CTG TGT GGG ATC CAG CTG GTG AAC GCG ACC ATT   583
Cys Leu Glu Ile Val Leu Cys Gly Ile Gln Leu Val Asn Ala Thr Ile
            170   175   180
GGT GTC TTC TGC GGC GAT TGC AGG AAA AAA CAG GAC ACC CCT CAC TG   630
Gly Val Phe Cys Gly Asp Cys Arg Lys Lys Gln Asp Thr Pro His
        185   190   195
AGGCTCCACT GACCGCCGGG TTACACCTGC TCCTTCCTGG ACGCCTACCT GGCTCGCTCA   690
CTCCCTTGCT CGCTAGAATA AACTGCTTTG CGCTCTCTT   729

(2) INFORMATION FOR SEQ ID NO: 41:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1322

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP01526

(ix) SEQUENCE CHARACTERISTICS:

(A) CHARACTERIZATION CODE: CDS

(B) EXISTENCE POSITION: 84.. 749

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

```
GAGCCGCAGG TCTGGGCTGC AGTAGGTCCC GGCAACCGCA GGCTCGCGGC GGGCGCTGGG      60
CGCGGGATCC GACTCTAGTC GTA ATG GAG GCG GGC GGC TTT CTG GAC TCG CTC      113
                          Met Glu Ala Gly Gly Phe Leu Asp Ser Leu
                            1               5                  10
ATT TAC GGA GCA TGC GTG GTC TTC ACC CTT GGC ATG TTC TCC GCC GGC        161
Ile Tyr Gly Ala Cys Val Val Phe Thr Leu Gly Met Phe Ser Ala Gly
                    15                  20                  25
CTC TCG GAC CTC AGG CAC ATG CGA ATG ACC CGG AGT GTG GAC AAC GTC        209
Leu Ser Asp Leu Arg His Met Arg Met Thr Arg Ser Val Asp Asn Val
                30                  35                  40
CAG TTC CTG CCC TTT CTC ACC ACG GAA GTC AAC AAC CTG GGC TGG CTG        257
Gln Phe Leu Pro Phe Leu Thr Thr Glu Val Asn Asn Leu Gly Trp Leu
        45                  50                  55
AGT TAT GGG GCT TTG AAG GGA GAC GGG ATC CTC ATC GTC GTC AAC ACA        305
Ser Tyr Gly Ala Leu Lys Gly Asp Gly Ile Leu Ile Val Val Asn Thr
    60                  65                  70
GTG GGT GCT GCG CTT CAG ACC CTG TAT ATC TTG GCA TAT CTG CAT TAC        353
Val Gly Ala Ala Leu Gln Thr Leu Tyr Ile Leu Ala Tyr Leu His Tyr
 75                  80                  85                  90
TGC CCT CGG AAG CGT GTT GTG CTC CTA CAG ACT GCA ACC CTG CTA GGG        401
Cys Pro Arg Lys Arg Val Val Leu Leu Gln Thr Ala Thr Leu Leu Gly
                95                  100                 105
GTC CTT CTC CTG GGT TAT GGC TAC TTT TGG CTC CTG GTA CCC AAC CCT        449
Val Leu Leu Leu Gly Tyr Gly Tyr Phe Trp Leu Leu Val Pro Asn Pro
            110                 115                 120
GAG GCC CGG CTT CAG CAG TTG GGC CTC TTC TGC AGT GTC TTC ACC ATC        497
Glu Ala Arg Leu Gln Gln Leu Gly Leu Phe Cys Ser Val Phe Thr Ile
        125                 130                 135
AGC ATG TAC CTC TCA CCA CTG GCT GAC TTG GCT AAG GTG ATT CAA ACT        545
Ser Met Tyr Leu Ser Pro Leu Ala Asp Leu Ala Lys Val Ile Gln Thr
    140                 145                 150
AAA TCA ACC CAA TGT CTC TCC TAC CCA CTC ACC ATT GCT ACC CTT CTC        593
Lys Ser Thr Gln Cys Leu Ser Tyr Pro Leu Thr Ile Ala Thr Leu Leu
155                 160                 165                 170
ACC TCT GCC TCC TGG TGC CTC TAT GGG TTT CGA CTC AGA GAT CCC TAT        641
Thr Ser Ala Ser Trp Cys Leu Tyr Gly Phe Arg Leu Arg Asp Pro Tyr
```

```
                    175                 180                 185
ATC ATG GTG TCC AAC TTT CCA GGA ATC GTC ACC AGC TTT ATC CGC TTC      689
Ile Met Val Ser Asn Phe Pro Gly Ile Val Thr Ser Phe Ile Arg Phe
            190                 195                 200
TGG CTT TTC TGG AAG TAC CCC CAG GAG CAA GAC AGG AAC TAC TGG CTC      737
Trp Leu Phe Trp Lys Tyr Pro Gln Glu Gln Asp Arg Asn Tyr Trp Leu
        205                 210                 215
CTG CAA ACC TGAGGCTGCT CATCTGACCA CTGGGCACCT TAGTGCCAAC CTGA         790
Leu Gln Thr
    220
ACCAAAGAGA CCTCCTTGTT TCAGCTGGGC CTGCTGTCCA GCTTCCCAGG TGCAGTGGGT    850
TGTGGGAACA AGAGATGACT TTGAGGATAA AAGGACCAAA GAAAAAGCTT TACTTAGATG    910
ATTGATTGGG GCCTAGGAGA TGAAATCACT TTTTATTTTT TAGAGATTTT TTTTTTTAAT    970
TTTGGAGGTT GGGGTGCAAT CTTTAGAATA TGCCTTAAAA GGCCGGGCGC GGTGGCTCAC   1030
GCCTGTAATC CCAGCACTTT GGGAGGCCAA GGTGGGCGGA TCGCCTGAGG TCAGGAGTTC   1090
AAGACCAACC TGACTAACAT GGTGAAACCC CATCTCTACT AAAAATACAA AATTAGCCAG   1150
GCATGATGGC ACATGCCTGT AATCCCAGAT ACTTGGGAGG CTGAGGCAGG AGAATTGCTT   1210
GAACCCAGGA GGTGGAGGTT GCAGTGAGCT GAGATCGTGC CATTGTGATA TGAATATGCC   1270
TTATATGCTG ATATGAATAT GCCTTAAAAT AAAGTGTTCC CCACCCCTGC CC           1322
```

(2) INFORMATION FOR SEQ ID NO: 42:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 3045

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10230

(ix) SEQUENCE CHARACTERISTICS:

(A) CHARACTERIZATION CODE: CDS

(B) EXISTENCE POSITION: 191.. 946

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

```
GTTTCGCCTC AGAAGGCTGC CTCGCTGGTC CGAATTCGGT GGCGCCACGT CCGCCCGTCT    60
CCGCCTTCTG CATCGCGGCT TCGGCGGCTT CCACCTAGAC ACCTAACAGT CGCGGAGCCG   120
GCCGCGTCGT GAGGGGGTCG GCACGGGGAG TCGGGCGGTC TTGTGCATCT TGGCTACCTG   180
TGGGTCGAAG ATG TCG GAC ATC GGA GAC TGG TTC AGG AGC ATC CCG GCG      229
           Met Ser Asp Ile Gly Asp Trp Phe Arg Ser Ile Pro Ala
             1               5                  10
ATC ACG CGC TAT TGG TTC GCC GCC ACC GTC GCC GTG CCC TTG GTC GGC     277
Ile Thr Arg Tyr Trp Phe Ala Ala Thr Val Ala Val Pro Leu Val Gly
     15                  20                  25
AAA CTC GGC CTC ATC AGC CCG GCC TAC CTC TTC CTC TGG CCC GAA GCC     325
Lys Leu Gly Leu Ile Ser Pro Ala Tyr Leu Phe Leu Trp Pro Glu Ala
 30                  35                  40                  45
TTC CTT TAT CGC TTT CAG ATT TGG AGG CCA ATC ACT GCC ACC TTT TAT     373
Phe Leu Tyr Arg Phe Gln Ile Trp Arg Pro Ile Thr Ala Thr Phe Tyr
                 50                  55                  60
TTC CCT GTG GGT CCA GGA ACT GGA TTT CTT TAT TTG GTC AAT TTA TAT     421
Phe Pro Val Gly Pro Gly Thr Gly Phe Leu Tyr Leu Val Asn Leu Tyr
             65                  70                  75
TTC TTA TAT CAG TAT TCT ACG CGA CTT GAA ACA GGA GCT TTT GAT GGG     469
Phe Leu Tyr Gln Tyr Ser Thr Arg Leu Glu Thr Gly Ala Phe Asp Gly
         80                  85                  90
AGG CCA GCA GAC TAT TTA TTC ATG CTC CTC TTT AAC TGG ATT TGC ATC     517
Arg Pro Ala Asp Tyr Leu Phe Met Leu Leu Phe Asn Trp Ile Cys Ile
     95                 100                 105
GTG ATT ACT GGC TTA GCA ATG GAT ATG CAG TTG CTG ATG ATT CCT CTG     565
Val Ile Thr Gly Leu Ala Met Asp Met Gln Leu Leu Met Ile Pro Leu
110                 115                 120                 125
ATC ATG TCA GTA CTT TAT GTC TGG GCC CAG CTG AAC AGA GAC ATG ATT     613
Ile Met Ser Val Leu Tyr Val Trp Ala Gln Leu Asn Arg Asp Met Ile
                130                 135                 140
GTA TCA TTT TGG TTT GGA ACA CGA TTT AAG GCC TGC TAT TTA CCC TGG     661
Val Ser Phe Trp Phe Gly Thr Arg Phe Lys Ala Cys Tyr Leu Pro Trp
            145                 150                 155
GTT ATC CTT GGA TTC AAC TAT ATC ATC GGA GGC TCG GTA ATC AAT GAG     709
Val Ile Leu Gly Phe Asn Tyr Ile Ile Gly Gly Ser Val Ile Asn Glu
        160                 165                 170
```

CTT ATT GGA AAT CTG GTT GGA CAT CTT TAT TTT TTC CTA ATG TTC AGA 757
Leu Ile Gly Asn Leu Val Gly His Leu Tyr Phe Phe Leu Met Phe Arg
175 180 185

TAC CCA ATG GAC TTG GGA GGA AGA AAT TTT CTA TCC ACA CCT CAG TTT 805
Tyr Pro Met Asp Leu Gly Gly Arg Asn Phe Leu Ser Thr Pro Gln Phe
190 195 200 205

TTG TAC CGC TGG CTG CCC AGT AGG AGA GGA GGA GTA TCA GGA TTT GGT 853
Leu Tyr Arg Trp Leu Pro Ser Arg Arg Gly Gly Val Ser Gly Phe Gly
210 215 220

GTG CCC CCT GCT AGC ATG AGG CGA GCT GCT GAT CAG AAT GGC GGA GGC 901
Val Pro Pro Ala Ser Met Arg Arg Ala Ala Asp Gln Asn Gly Gly Gly
225 230 235

GGG AGA CAC AAC TGG GGC CAG GGC TTT CGA CTT GGA GAC CAG TGAAGGG 950
Gly Arg His Asn Trp Gly Gln Gly Phe Arg Leu Gly Asp Gln
240 245 250

GCGGCCTCGG GCAGCCGCTC CTCTCAAGCC ACATTTCCTC CCAGTGCTGG GTGCGCTTAA 1010
CAACTGCGTT CTGGCTAACA CTGTTGGACC TGACCCACAC TGAATGTAGT CTTTCAGTAC 1070
GAGACAAAGT TTCTTAAATC CCGAAGAAAA ATATAAGTGT TCCACAAGTT TCACGATTCT 1130
CATTCAAGTC CTTACTGCTG TGAAGAACAA ATACCAACTG TGCAAATTGC AAAACTGACT 1190
ACATTTTTTG GTGTCTTCTC TTCTCCCCTT TCCGTCTGAA TAATGGGTTT TAGCGGGTCC 1250
TAGTCTGCTG GCATTGAGCT GGGGCTGGGT CACCAAACCC TTCCCAAAAG GACCCTTATC 1310
TCTTTCTTGC ACACATGCCT CTCTCCCACT TTTCCCAACC CCCACATTTG CAACTAGAAG 1370
AGGTTGCCCA TAAAATTGCT CTGCCCTTGA CAGGTTCTGT TATTTATTGA CTTTTGCCAA 1430
GGCTTGGTCA CAACAATCAT ATTCACGTAA TTTTCCCCCT TTGGTGGCAG AACTGTAGCA 1490
ATAGGGGGAG AAGACAAGCA GCGGATGAAG CGTTTTCTCA GCTTTTGGAA TTGCTTCGAC 1550
CTGACATCCG TTGTAACCGT TTGCCACTTC TTCAGATATT TTTATAAAAA AGTACCACTG 1610
AGTCAGTGAG GGCCACAGAT TGGTATTAAT GAGATACGAG GGTTGTTGCT GGGTGTTTGT 1670
TTCCTGAGCT AAGTGATCAA GACTGTAGTG GAGTTGCAGC TAACATGGGT TAGGTTTAAA 1730
CCGTGGGGGA TGCAACCCCT TTGCGTTTCA TATGTAGGCC TACTGGCTTT GTGTAGCTGG 1790
AGTAGTTGGG TTGCTTTGTG TTAGGAGGAT CCAGATCATG TTGGCTACAG GGAGATGCTC 1850
TCTTTGAGAG GCTCCTGGGC ATTGATTCCA TTTCAATCTC ATTCTGGATA TGTGTTCATT 1910
GAGTAAAGGA GGAGAGACCC TCATACGCTA TTTAAATGTC ACTTTTTTGC CTATCCCCCG 1970
TTTTTTGGTC ATGTTTCAAT TAATTGTGAG GAAGGCGCAG CTCCTCTCTG CACGTAGATC 2030
ATTTTTTAAA GCTAATGTAA GCACATCTAA GGGAATAACA TGATTTAAGG TTGAAATGGC 2090
TTTAGAATCA TTTGGGTTTG AGGGTGTGTT ATTTTGAGTC ATGAATGTAC AAGCTCTGTG 2150
AATCAGACCA GCTTAAATAC CCACACCTTT TTTTCGTAGG TGGGCTTTTC CTATCAGAGC 2210
TTGGCTCATA ACCAAATAAA GTTTTTTGAA GGCCATGGCT TTTCACACAG TTATTTTATT 2270
TTATGACGTT ATCTGAAAGC AGACTGTTAG GAGCAGTATT GAGTGGCTGT CACACTTTGA 2330

```
GGCAACTAAA AAGGCTTCAA ACGTTTTGAT CAGTTTCTTT TCAGGAAACA TTGTGCTCTA   2390
ACAGTATGAC TATTCTTTCC CCCACTCTTA AACAGTGTGA TGTGTGTTAT CCTAGGAAAT   2450
GAGAGTTGGC AAACAACTTC TCATTTTGAA TAGAGTTTGT GTGTACCTCT CCATATTTAA   2510
TTTATATGAT AAAATAGGTG GGGAGAGTCT GAACCTTAAC TGTCATGTTT TGTTGTTCAT   2570
CTGTGGCCAC AATAAAGTTT ACTTGTAAAA TTTTAGAGGC CATTACTCCA ATTATGTTGC   2630
ACGTACACTC ATTGTACAGG CGTGGAGACT CATTGTATGT ATAAGAATAT TCTGACAGTG   2690
AGTGACCCGG AGTCTCTGGT GTACCCTCTT ACCAGTCAGC TGCCTGCGAG CAGTCATTTT   2750
TTCCTAAAGG TTTACAAGTA TTTAGAACTC TTCAGTTCAG GGCAAAATGT TCATGAAGTT   2810
ATTCCTCTTA AACATGGTTA GGAAGCTGAT GACGTTATTG ATTTTGTCTG GATTATGTTT   2870
CTGGAATAAT TTTACCAAAA CAAGCTATTT GAGTTTTGAC TTGACAAGGC AAAACATGAC   2930
AGTGGATTCT CTTTACAAAT TGAAAAAAAA AATCCTTATT TTGTATAAAG GACTTCCCTT   2990
TTTGTAAACT AATCCTTTTT ATTGGTAAAA ATTGTAAATT AAAATGTGCA ACTTG        3045
```

(2) INFORMATION FOR SEQ ID NO: 43:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 653

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Epidermoid carcinoma

(C) CELL LINE: KB

(D) CLONE NAME: HP10389

(ix) SEQUENCE CHARACTERISTICS:

(A) CHARACTERIZATION CODE: CDS

(B) EXISTENCE POSITION: 63.. 383

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

```
ATGACCTTCA CCGGGAGGCT GAGGTCGGAG TCCCGATTTT CTCCTGCTGC TGTGGCCCGG     60
AC ATG GCG ACT CCC GGC CCT GTG ATT CCG GAG GTC CCC TTT GAA CCA      107
   Met Ala Thr Pro Gly Pro Val Ile Pro Glu Val Pro Phe Glu Pro
```

```
      1               5                  10                 15
TCG AAG CCT CCA GTC ATT GAG GGG CTG AGC CCC ACT GTT TAC AGG AAT      155
Ser Lys Pro Pro Val Ile Glu Gly Leu Ser Pro Thr Val Tyr Arg Asn
                 20                  25                  30
CCA GAG AGT TTC AAG GAA AAG TTC GTT CGC AAG ACC CGC GAG AAC CCG      203
Pro Glu Ser Phe Lys Glu Lys Phe Val Arg Lys Thr Arg Glu Asn Pro
             35                  40                  45
GTG GTA CCC ATA GGT TGC CTG GCC ACG GCG GCC GCC CTC ACC TAC GGC      251
Val Val Pro Ile Gly Cys Leu Ala Thr Ala Ala Ala Leu Thr Tyr Gly
         50                  55                  60
CTC TAC TCC TTC CAC CGG GGC AAC AGC CAG CGC TCT CAG CTC ATG ATG      299
Leu Tyr Ser Phe His Arg Gly Asn Ser Gln Arg Ser Gln Leu Met Met
     65                  70                  75
CGC ACC CGG ATC GCC GCC CAG GGT TTC ACG GTC GCA GCC ATC TTG CTG      347
Arg Thr Arg Ile Ala Ala Gln Gly Phe Thr Val Ala Ala Ile Leu Leu
 80                  85                  90                  95
GGT CTG GCT GTC ACT GCT ATG AAG TCT CGA CCC TAAGCCCAGG GTCTGGCCTT    400
Gly Leu Ala Val Thr Ala Met Lys Ser Arg Pro
                100                 105
GAAAGCTCCG CAGAAATGAT TCCAAAACCC AGGGAGCAAC CACTGGCCCT ACCGTGGGAC    460
TTACTCCCTC CTCTCCTTTG AGAGGCCCAT GTGTCGCTGG GGAGGAAGTG ACCCTTTGTG    520
TAACTGTAAC CGAAAGTTTT TTCAAAAATC CTAGATGCTG TTGTTTGAAT GTTACATACT    580
TCTATTTGTG CCACATCTCC CCTCCACTCC CCTGCTTAAT AAACTCTAAA AATCCACTTG    640
TATTTAATTC AGT                                                       653
```

(2) INFORMATION FOR SEQ ID NO: 44:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 439

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10408

(ix) SEQUENCE CHARACTERISTICS:
(A) CHARACTERIZATION CODE: CDS
(B) EXISTENCE POSITION: 75.. 311
(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:

```
GTAGAAACAG GCCTGTTAAG GAGAGGCCAC CGGGACTTCA GTGTCTCCTC CATCCCAGGA      60
GCGCAGTGGC CACT ATG GGG TCT GGG CTG CCC CTT GTC CTC CTC TTG ACC        110
                Met Gly Ser Gly Leu Pro Leu Val Leu Leu Leu Thr
                  1               5                  10
CTC CTT GGC AGC TCA CAT GGA ACA GGG CCG GGT ATG ACT TTG CAA CTG        158
Leu Leu Gly Ser Ser His Gly Thr Gly Pro Gly Met Thr Leu Gln Leu
            15                  20                  25
AAG CTG AAG GAG TCT TTT CTG ACA AAT TCC TCC TAT GAG TCC AGC TTC        206
Lys Leu Lys Glu Ser Phe Leu Thr Asn Ser Ser Tyr Glu Ser Ser Phe
        30                  35                  40
CTG GAA TTG CTT GAA AAG CTC TGC CTC CTC CTC CAT CTC CCT TCA GGG        254
Leu Glu Leu Leu Glu Lys Leu Cys Leu Leu Leu His Leu Pro Ser Gly
 45                  50                  55                  60
ACC AGC GTC ACC CTC CAC CAT GCA AGA TCT CAA CAC CAT GTT GTC TGC        302
Thr Ser Val Thr Leu His His Ala Arg Ser Gln His His Val Val Cys
                    65                  70                  75
AAC ACA TGACAGCCAT TGAAGCCTGT GTCCTTCTTG GCCCGGGCTT TTGGGCCGGG GA      360
Asn Thr

TGCAGGAGGC AGGCCCCGAC CCTGTCTTTC AGCAGGCCCC CACCCTCCTG AGTGGCAATA      420
AATAAAATTC GGTATGCTG                                                   439
```

(2) INFORMATION FOR SEQ ID NO: 45:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1131
(B) TYPE: Nucleic acid
(C) STRANDEDNESS: Double
(D) TOPOLOGY: Linear
(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:
(A) ORGANISM: *Homo sapiens*
(B) CELL KIND: Stomach cancer
(D) CLONE NAME: HP10412

(ix) SEQUENCE CHARACTERISTICS:
(A) CHARACTERIZATION CODE: CDS
(B) EXISTENCE POSITION: 56.. 1000
(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45:

```
CTATGAGATC CCGGCCTCAG GGTGGACGCA GTGGTTCTGC ACTGAGGCCC TCGTC ATG      58
                                                                 Met
                                                                   1
GTG GCG CCT GTG TGG TAC TTG GTA GCG GCG GCT CTG CTA GTC GGC TTT      106
Val Ala Pro Val Trp Tyr Leu Val Ala Ala Ala Leu Leu Val Gly Phe
               5                  10                  15
ATC CTC TTC CTG ACT CGC AGC CGG GGC CGG GCG GCA TCA GCC GGC CAA      154
Ile Leu Phe Leu Thr Arg Ser Arg Gly Arg Ala Ala Ser Ala Gly Gln
           20                  25                  30
GAG CCA CTG CAC AAT GAG GAG CTG GCA GGA GCA GGC CGG GTG GCC CAG      202
Glu Pro Leu His Asn Glu Glu Leu Ala Gly Ala Gly Arg Val Ala Gln
       35                  40                  45
CCT GGG CCC CTG GAG CCT GAG GAG CCG AGA GCT GGA GGC AGG CCT CGG      250
Pro Gly Pro Leu Glu Pro Glu Glu Pro Arg Ala Gly Gly Arg Pro Arg
   50                  55                  60                  65
CGC CGG AGG GAC CTG GGC AGC CGC CTA CAG GCC CAG CGT CGA GCC CAG      298
Arg Arg Arg Asp Leu Gly Ser Arg Leu Gln Ala Gln Arg Arg Ala Gln
               70                  75                  80
CGG GTG GCC TGG GCA GAA GCA GAT GAG AAC GAG GAG GAA GCT GTC ATC      346
Arg Val Ala Trp Ala Glu Ala Asp Glu Asn Glu Glu Glu Ala Val Ile
           85                  90                  95
CTA GCC CAG GAG GAG GAA GGT GTC GAG AAG CCA GCG GAA ACT CAC CTG      394
Leu Ala Gln Glu Glu Glu Gly Val Glu Lys Pro Ala Glu Thr His Leu
       100                 105                 110
TCG GGG AAA ATT GGA GCT AAG AAA CTG CGG AAG CTG GAG GAG AAA CAA      442
Ser Gly Lys Ile Gly Ala Lys Lys Leu Arg Lys Leu Glu Glu Lys Gln
```

```
    115                     120                     125
GCG CGA AAG GCC CAG CGT GAG GCA GAG GAG GCT GAA CGT GAG GAG CGG      490
Ala Arg Lys Ala Gln Arg Glu Ala Glu Glu Ala Glu Arg Glu Glu Arg
130                     135                     140                     145
AAA CGA CTC GAG TCC CAG CGC GAA GCT GAG TGG AAG AAG GAG GAG GAG      538
Lys Arg Leu Glu Ser Gln Arg Glu Ala Glu Trp Lys Lys Glu Glu Glu
                150                     155                     160
CGG CTT CGC CTG GAG GAG GAG CAG AAG GAG GAG GAG GAG AGG AAG GCC      586
Arg Leu Arg Leu Glu Glu Glu Gln Lys Glu Glu Glu Glu Arg Lys Ala
            165                     170                     175
CGC GAG GAG CAG GCC CAG CGG GAG CAT GAG GAG TAC CTG AAA CTG AAG      634
Arg Glu Glu Gln Ala Gln Arg Glu His Glu Glu Tyr Leu Lys Leu Lys
        180                     185                     190
GAG GCC TTT GTG GTG GAG GAG GAA GGC GTA GGA GAG ACC ATG ACT GAG      682
Glu Ala Phe Val Val Glu Glu Glu Gly Val Gly Glu Thr Met Thr Glu
    195                     200                     205
GAA CAG TCC CAG AGC TTC CTG ACA GAG TTC ATC AAC TAC ATC AAG CAG      730
Glu Gln Ser Gln Ser Phe Leu Thr Glu Phe Ile Asn Tyr Ile Lys Gln
210                     215                     220                     225
TCC AAG GTT GTG CTC TTG GAA GAC CTG GCT TCC CAG GTG GGC CTA CGC      778
Ser Lys Val Val Leu Leu Glu Asp Leu Ala Ser Gln Val Gly Leu Arg
                230                     235                     240
ACT CAG GAC ACC ATA AAT CGC ATC CAG GAC CTG CTG GCT GAG GGG ACT      826
Thr Gln Asp Thr Ile Asn Arg Ile Gln Asp Leu Leu Ala Glu Gly Thr
            245                     250                     255
ATA ACA GGT GTG ATT GAC GAC CGG GGC AAG TTC ATC TAC ATA ACC CCA      874
Ile Thr Gly Val Ile Asp Asp Arg Gly Lys Phe Ile Tyr Ile Thr Pro
        260                     265                     270
GAG GAA CTG GCC GCC GTG GCC AAC TTC ATC CGA CAG CGG GGC CGG GTG      922
Glu Glu Leu Ala Ala Val Ala Asn Phe Ile Arg Gln Arg Gly Arg Val
    275                     280                     285
TCC ATC GCC GAG CTT GCC CAA GCC AGC AAC TCC CTC ATC GCC TGG GGC      970
Ser Ile Ala Glu Leu Ala Gln Ala Ser Asn Ser Leu Ile Ala Trp Gly
290                     295                     300                     305
CGG GAG TCC CCT GCC CAA GCC CCA GCC TGACCCCAGT CCTTCCCTCT TGG       1020
Arg Glu Ser Pro Ala Gln Ala Pro Ala
                310
ACTCAGAGTT GGTGTGGCCT ACCTGGCTAT ACATCTTCAT CCCTCCCCAC CATCCTGGGG   1080
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AAGTGATGGT GTGGCCAGGC AGTTATAGAT TAAAGGCCTG TGAGTACTGC T 1131

(2) INFORMATION FOR SEQ ID NO: 46:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1875

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10413

(ix) SEQUENCE CHARACTERISTICS:

(A) CHARACTERIZATION CODE: CDS

(B) EXISTENCE POSITION: 79.. 666

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:

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CTCGCTCGCT CAGAGGGAGG AGAAAGTGGC GAGTTCCGGA TCCCTGCCTA GCGCGGCCCA      60
ACCTTTACTC CAGAGATC ATG GCT GCC GAG GAT GTG GTG GCG ACT GGC GCC       111
                    Met Ala Ala Glu Asp Val Val Ala Thr Gly Ala
                      1               5                  10
GAC CCA AGC GAT CTG GAG AGC GGC GGG CTG CTG CAT GAG ATT TTC ACG       159
Asp Pro Ser Asp Leu Glu Ser Gly Gly Leu Leu His Glu Ile Phe Thr
            15                  20                  25
TCG CCG CTC AAC CTG CTG CTG CTT GGC CTC TGC ATC TTC CTG CTC TAC       207
Ser Pro Leu Asn Leu Leu Leu Leu Gly Leu Cys Ile Phe Leu Leu Tyr
        30                  35                  40
AAG ATC GTG CGC GGG GAC CAG CCG GCG GCC AGC GGC GAC AGC GAC GAC       255
Lys Ile Val Arg Gly Asp Gln Pro Ala Ala Ser Gly Asp Ser Asp Asp
    45                  50                  55
GAC GAG CCG CCC CCT CTG CCC CGC CTC AAG CGG CGC GAC TTC ACC CCC       303
Asp Glu Pro Pro Pro Leu Pro Arg Leu Lys Arg Arg Asp Phe Thr Pro
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 60                  65                  70                  75
GCC GAG CTG CGG CGC TTC GAC GGC GTC CAG GAC CCG CGC ATA CTC ATG      351
Ala Glu Leu Arg Arg Phe Asp Gly Val Gln Asp Pro Arg Ile Leu Met
                 80                  85                  90
GCC ATC AAC GGC AAG GTG TTC GAT GTG ACC AAA GGC CGC AAA TTC TAC      399
Ala Ile Asn Gly Lys Val Phe Asp Val Thr Lys Gly Arg Lys Phe Tyr
            95                  100                 105
GGG CCC GAG GGG CCG TAT GGG GTC TTT GCT GGA AGA GAT GCA TCC AGG      447
Gly Pro Glu Gly Pro Tyr Gly Val Phe Ala Gly Arg Asp Ala Ser Arg
        110                 115                 120
GGC CTT GCC ACA TTT TGC CTG GAT AAG GAA GCA CTG AAG GAT GAG TAC      495
Gly Leu Ala Thr Phe Cys Leu Asp Lys Glu Ala Leu Lys Asp Glu Tyr
    125                 130                 135
GAT GAC CTT TCT GAC CTC ACT GCT GCC CAG CAG GAG ACT CTG AGT GAC      543
Asp Asp Leu Ser Asp Leu Thr Ala Ala Gln Gln Glu Thr Leu Ser Asp
140                 145                 150                 155
TGG GAG TCT CAG TTC ACT TTC AAG TAT CAT CAC GTG GGC AAA CTG CTG      591
Trp Glu Ser Gln Phe Thr Phe Lys Tyr His His Val Gly Lys Leu Leu
                160                 165                 170
AAG GAG GGG GAG GAG CCC ACT GTG TAC TCA GAT GAG GAA GAA CCA AAA      639
Lys Glu Gly Glu Glu Pro Thr Val Tyr Ser Asp Glu Glu Glu Pro Lys
            175                 180                 185
GAT GAG AGT GCC CGG AAA AAT GAT TAAAGCATTC AGTGGAAGTA TATCTAT        690
Asp Glu Ser Ala Arg Lys Asn Asp
        190                 195
TTTTGTATTT TGCAAAATCA TTTGTAACAG TCCACTCTGT CTTTAAAACA TAGTGATTAC    750
AATATTTAGA AAGTTTTGAG CACTTGCTAT AAGTTTTTTA TAACATCACT AGTGACACTA    810
ATAAAATTAA CTTCTTAGAA TGCATGATGT GTTTGTGTGT CACAAATCCA GAAAGTGAAC    870
TGCAGTGCTG TAATACACAT GTTAATACTG TTTTTCTTCT ATCTGTAGTT AGTACAGGAT    930
GAATTTAAAT GTGTTTTTCC TGAGAGACAA GGAAGACTTG GGTATTTCCC AAAACAGGTA    990
AAAATCTTAA ATGTGCACCA AGAGCAAAGG ATCAACTTTT AGTCATGATG TTCTGTAAAG   1050
ACAACAAATC CCTTTTTTTT TCTCAATTGA CTTAACTGCA TGATTTCTGT TTTATCTACC   1110
TCTAAAGCAA ATCTGCAGTG TTCCAAAGAC TTTGGTATGG ATTAAGCGCT GTCCAGTAAC   1170
AAAATGAAAT CTCAAAACAG AGCTCAGCTG CAAAAAAGCA TATTTTCTGT GTTTCTGGAC   1230
TGCACTGTTG TCCTTGCCCT CACATAGACA CTCAGACACC CTCACAAACA CAGTAGTCTA   1290
TAGTTAGGAT TAAAATAGGA TCTGAACATT CAAAAGAAAG CTTTGGAAAA AAAGAGCTGG   1350
CTGGCCTAAA AACCTAAATA TATGATGAAG ATTGTAGGAC TGTCTTCCCA AGCCCCATGT   1410
TCATGGTGGG GCAATGGTTA TTTGGTTATT TTACTCAATT GGTTACTCTC ATTTGAAATG   1470
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AGGGAGGGAC ATACAGAATA GGAACAGGTG TTTGCTCTCC TAAGAGCCTT CATGCACACC 1530
CCTGAACCAC GAGGAAACAG TACAGTCGCT AGTCAAGTGG TTTTTAAAGT AAAGTATATT 1590
CATAAGGTAA CAGTTATTCT GTTGTTATAA AACTATACCC ACTGCAAAAG TAGTAGTCAA 1650
GTGTCTAGGT CTTTGATATT GCTCTTTTGG TTAACACTAA GCTTAAGTAG ACTATACAGT 1710
TGTATGAATT TGTAAAAGTA TATGAACACC TAGTGAGATT TCAAACTTGT AATTGTGGTT 1770
AAATAGTCAT TGTATTTTCT TGTGAACTGT GTTTTATGAT TTTACCTCAA ATCAGAAAAC 1830
AAAATGATGT GCTTTGGTCA GTTAATAAAA ATGGTTTTAC CCACT 1875

(2) INFORMATION FOR SEQ ID NO: 47:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1563

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10415

(ix) SEQUENCE CHARACTERISTICS:

(A) CHARACTERIZATION CODE: CDS

(B) EXISTENCE POSITION: 72.. 1460

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:

AAATTGGGCC AGGCTGAGGC GCTGCTGCTG GAGCGGCCGA TCCGAGACGT GGCTCCCTGG 60
GCGGCAGAAC C ATG TTG GAC TTC GCG ATC TTC GCC GTT ACC TTC TTG CTG 110
Met Leu Asp Phe Ala Ile Phe Ala Val Thr Phe Leu Leu
1 5 10
GCG TTG GTG GGA GCC GTG CTC TAC CTC TAT CCG GCT TCC AGA CAA GCT 158
Ala Leu Val Gly Ala Val Leu Tyr Leu Tyr Pro Ala Ser Arg Gln Ala
15 20 25
GCA GGA ATT CCA GGG ATT ACT CCA ACT GAA GAA AAA GAT GGT AAT CTT 206
Ala Gly Ile Pro Gly Ile Thr Pro Thr Glu Glu Lys Asp Gly Asn Leu

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     30                  35                  40                  45
     CCA GAT ATT GTG AAT AGT GGA AGT TTG CAT GAG TTC CTG GTT AAT TTG      254
     Pro Asp Ile Val Asn Ser Gly Ser Leu His Glu Phe Leu Val Asn Leu
                     50                  55                  60
 5   CAT GAG AGA TAT GGG CCT GTG GTC TCC TTC TGG TTT GGC AGG CGC CTC      302
     His Glu Arg Tyr Gly Pro Val Val Ser Phe Trp Phe Gly Arg Arg Leu
                 65                  70                  75
     GTG GTT AGT TTG GGC ACT GTT GAT GTA CTG AAG CAG CAT ATC AAT CCC      350
     Val Val Ser Leu Gly Thr Val Asp Val Leu Lys Gln His Ile Asn Pro
10           80                  85                  90
     AAT AAG ACA TTG GAC CCT TTT GAA ACC ATG CTG AAG TCA TTA TTA AGG      398
     Asn Lys Thr Leu Asp Pro Phe Glu Thr Met Leu Lys Ser Leu Leu Arg
          95                 100                 105
     TAT CAA TCT GGT GGT GGC AGT GTG AGT GAA AAC CAC ATG AGG AAA AAA      446
15   Tyr Gln Ser Gly Gly Gly Ser Val Ser Glu Asn His Met Arg Lys Lys
     110                 115                 120                 125
     TTG TAT GAA AAT GGT GTG ACT GAT TCT CTG AAG AGT AAC TTT GCC CTC      494
     Leu Tyr Glu Asn Gly Val Thr Asp Ser Leu Lys Ser Asn Phe Ala Leu
                     130                 135                 140
20   CTC CTA AAG CTT TCA GAA GAA TTA TTA GAT AAA TGG CTC TCC TAC CCA      542
     Leu Leu Lys Leu Ser Glu Glu Leu Leu Asp Lys Trp Leu Ser Tyr Pro
                 145                 150                 155
     GAG ACC CAG CAC GTG CCC CTC AGC CAG CAT ATG CTT GGT TTT GCT ATG      590
     Glu Thr Gln His Val Pro Leu Ser Gln His Met Leu Gly Phe Ala Met
25           160                 165                 170
     AAG TCT GTT ACA CAG ATG GTA ATG GGT AGT ACA TTT GAA GAT GAT CAG      638
     Lys Ser Val Thr Gln Met Val Met Gly Ser Thr Phe Glu Asp Asp Gln
          175                 180                 185
     GAA GTC ATT CGC TTC CAG AAG AAT CAT GGC ACA GTT TGG TCT GAG ATT      686
30   Glu Val Ile Arg Phe Gln Lys Asn His Gly Thr Val Trp Ser Glu Ile
     190                 195                 200                 205
     GGA AAA GGC TTT CTA GAT GGG TCA CTT GAT AAA AAC ATG ACT CGG AAA      734
     Gly Lys Gly Phe Leu Asp Gly Ser Leu Asp Lys Asn Met Thr Arg Lys
                     210                 215                 220
35   AAA CAA TAT GAA GAT GCC CTC ATG CAA CTG GAG TCT GTT TTA AGG AAC      782
     Lys Gln Tyr Glu Asp Ala Leu Met Gln Leu Glu Ser Val Leu Arg Asn
                 225                 230                 235
     ATC ATA AAA GAA CGA AAA GGA AGG AAC TTC AGT CAA CAT ATT TTC ATT      830
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Ile Ile Lys Glu Arg Lys Gly Arg Asn Phe Ser Gln His Ile Phe Ile
240 245 250

GAC TCC TTA GTA CAA GGG AAC CTT AAT GAC CAA CAG ATC CTA GAA GAC 878
Asp Ser Leu Val Gln Gly Asn Leu Asn Asp Gln Gln Ile Leu Glu Asp
255 260 265

AGT ATG ATA TTT TCT CTG GCC AGT TGC ATA ATA ACT GCA AAA TTG TGT 926
Ser Met Ile Phe Ser Leu Ala Ser Cys Ile Ile Thr Ala Lys Leu Cys
270 275 280 285

ACC TGG GCA ATC TGT TTT TTA ACC ACC TCT GAA GAA GTT CAA AAA AAA 974
Thr Trp Ala Ile Cys Phe Leu Thr Thr Ser Glu Glu Val Gln Lys Lys
290 295 300

TTA TAT GAA GAG ATA AAC CAA GTT TTT GGA AAT GGT CCT GTT ACT CCA 1022
Leu Tyr Glu Glu Ile Asn Gln Val Phe Gly Asn Gly Pro Val Thr Pro
305 310 315

GAG AAA ATT GAG CAG CTC AGA TAT TGT CAG CAT GTG CTT TGT GAA ACT 1070
Glu Lys Ile Glu Gln Leu Arg Tyr Cys Gln His Val Leu Cys Glu Thr
320 325 330

GTT CGA ACT GCC AAA CTG ACT CCA GTT TCT GCC CAG CTT CAA GAT ATT 1118
Val Arg Thr Ala Lys Leu Thr Pro Val Ser Ala Gln Leu Gln Asp Ile
335 340 345

GAA GGA AAA ATT GAC CGA TTT ATT ATT CCT AGA GAG ACC CTC GTC CTT 1166
Glu Gly Lys Ile Asp Arg Phe Ile Ile Pro Arg Glu Thr Leu Val Leu
350 355 360 365

TAT GCC CTT GGT GTG GTA CTT CAG GAT CCT AAT ACT TGG CCA TCT CCA 1214
Tyr Ala Leu Gly Val Val Leu Gln Asp Pro Asn Thr Trp Pro Ser Pro
370 375 380

CAC AAG TTT GAT CCA GAT CGG TTT GAT GAT GAA TTA GTA ATG AAA ACT 1262
His Lys Phe Asp Pro Asp Arg Phe Asp Asp Glu Leu Val Met Lys Thr
385 390 395

TTT TCC TCA CTT GGA TTC TCA GGC ACA CAG GAG TGT CCA GAG TTG AGG 1310
Phe Ser Ser Leu Gly Phe Ser Gly Thr Gln Glu Cys Pro Glu Leu Arg
400 405 410

TTT GCA TAT ATG GTG ACC ACA GTA CTT CTT AGT GTA TTG GTG AAG AGA 1358
Phe Ala Tyr Met Val Thr Thr Val Leu Leu Ser Val Leu Val Lys Arg
415 420 425

CTG CAC CTA CTT TCT GTG GAG GGA CAG GTT ATT GAA ACA AAG TAT GAA 1406
Leu His Leu Leu Ser Val Glu Gly Gln Val Ile Glu Thr Lys Tyr Glu
430 435 440 445

CTG GTA ACA TCA TCA AGG GAA GAA GCT TGG ATC ACT GTC TCA AAG AGA 1454
Leu Val Thr Ser Ser Arg Glu Glu Ala Trp Ile Thr Val Ser Lys Arg
450 455 460

TAT TAAAATTTTA TACATTTAAA ATCATTGTTA AATTGATTGA GGAAAACAAC CAT 1510
Tyr

TTAAAAAAAA TCTATGTTGA ATCCTTTTAT AAACCAGTAT CACTTTGTAA TAT 1563

(2) INFORMATION FOR SEQ ID NO: 48:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2030

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10419

(ix) SEQUENCE CHARACTERISTICS:

(A) CHARACTERIZATION CODE: CDS

(B) EXISTENCE POSITION: 171.. 914

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:

CATTTGGGGT TTCGGTTCCC CCCCTTCCCC TTCCCCGGGG TCTGGGGGTG ACATTGCACC 60
GCGCCCCTCG TGGGGTCGCG TTGCCACCCC ACGCGGACTC CCCAGCTGGC GCGCCCCTCC 120
CATTTGCCTG TCCTGGTCAG GCCCCCACCC CCCTTCCCAC CTGACCAGCC ATG GGG 176
Met Gly
1

GCT GCG GTG TTT TTC GGC TGC ACT TTC GTC GCG TTC GGC CCG GCC TTC 224
Ala Ala Val Phe Phe Gly Cys Thr Phe Val Ala Phe Gly Pro Ala Phe
5 10 15

GCG CTT TTC TTG ATC ACT GTG GCT GGG GAC CCG CTT CGC GTT ATC ATC 272

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Ala Leu Phe Leu Ile Thr Val Ala Gly Asp Pro Leu Arg Val Ile Ile
     20                  25                  30
CTG GTC GCA GGG GCA TTT TTC TGG CTG GTC TCC CTG CTC CTG GCC TCT      320
Leu Val Ala Gly Ala Phe Phe Trp Leu Val Ser Leu Leu Leu Ala Ser
 35                  40                  45                  50
GTG GTC TGG TTC ATC TTG GTC CAT GTG ACC GAC CGG TCA GAT GCC CGG      368
Val Val Trp Phe Ile Leu Val His Val Thr Asp Arg Ser Asp Ala Arg
                 55                  60                  65
CTC CAG TAC GGC CTC CTG ATT TTT GGT GCT GCT GTC TCT GTC CTT CTA      416
Leu Gln Tyr Gly Leu Leu Ile Phe Gly Ala Ala Val Ser Val Leu Leu
             70                  75                  80
CAG GAG GTG TTC CGC TTT GCC TAC TAC AAG CTG CTT AAG AAG GCA GAT      464
Gln Glu Val Phe Arg Phe Ala Tyr Tyr Lys Leu Leu Lys Lys Ala Asp
         85                  90                  95
GAG GGG TTA GCA TCG CTG AGT GAG GAC GGA AGA TCA CCC ATC TCC ATC      512
Glu Gly Leu Ala Ser Leu Ser Glu Asp Gly Arg Ser Pro Ile Ser Ile
    100                 105                 110
CGC CAG ATG GCC TAT GTT TCT GGT CTC TCC TTC GGT ATC ATC AGT GGT      560
Arg Gln Met Ala Tyr Val Ser Gly Leu Ser Phe Gly Ile Ile Ser Gly
115                 120                 125                 130
GTC TTC TCT GTT ATC AAT ATT TTG GCT GAT GCA CTT GGG CCA GGT GTG      608
Val Phe Ser Val Ile Asn Ile Leu Ala Asp Ala Leu Gly Pro Gly Val
                135                 140                 145
GTT GGG ATC CAT GGA GAC TCA CCC TAT TAC TTC CTG ACT TCA GCC TTT      656
Val Gly Ile His Gly Asp Ser Pro Tyr Tyr Phe Leu Thr Ser Ala Phe
            150                 155                 160
CTG ACA GCA GCC ATT ATC CTG CTC CAT ACC TTT TGG GGA GTT GTG TTC      704
Leu Thr Ala Ala Ile Ile Leu Leu His Thr Phe Trp Gly Val Val Phe
        165                 170                 175
TTT GAT GCC TGT GAG AGG AGA CGG TAC TGG GCT TTG GGC CTG GTG GTT      752
Phe Asp Ala Cys Glu Arg Arg Arg Tyr Trp Ala Leu Gly Leu Val Val
    180                 185                 190
GGG AGT CAC CTA CTG ACA TCG GGA CTG ACA TTC CTG AAC CCC TGG TAT      800
Gly Ser His Leu Leu Thr Ser Gly Leu Thr Phe Leu Asn Pro Trp Tyr
195                 200                 205                 210
GAG GCC AGC CTG CTG CCC ATC TAT GCA GTC ACT GTT TCC ATG GGG CTC      848
Glu Ala Ser Leu Leu Pro Ile Tyr Ala Val Thr Val Ser Met Gly Leu
                215                 220                 225
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TGG GCC TTC ATC ACA GCT GGA GGG TCC CTC CGA AGT ATT CAG CGC AGC 896
Trp Ala Phe Ile Thr Ala Gly Gly Ser Leu Arg Ser Ile Gln Arg Ser
230 235 240

CTC TTG TGT AAG GAC TGACTACCTG GACTGATCGC CTGACAGATC CCACCTGCC 950
Leu Leu Cys Lys Asp
245

TGTCCACTGC CCATGACTGA GCCCAGCCCC AGCCCGGGTC CATTGCCCAC ATTCTCTGTC 1010
TCCTTCTCGT CGGTCTACCC CACTACCTCC AGGGTTTTGC TTTGTCCTTT TGTGACCGTT 1070
AGTCTCTAAG CTTTACCAGG AGCAGCCTGG GTTCAGCCAG TCAGTGACTG GTGGGTTTGA 1130
ATCTGCACTT ATCCCCACCA CCTGGGGACC CCCTTGTTGT GTCCAGGACT CCCCCTGTGT 1190
CAGTGCTCTG CTCTCACCCT GCCCAAGACT CACCTCCCTT CCCCTCTGCA GGCCGACGGC 1250
AGGAGGACAG TCGGGTGATG GTGTATTCTG CCCTGCGCAT CCCACCCGAG GACTGAGGGA 1310
ACCTAGGGGG GACCCCTGGG CCTGGGGTGC CCTCCTGATG TCCTCGCCCT GTATTTCTCC 1370
ATCTCCAGTT CTGGACAGTG CAGGTTGCCA AGAAAAGGGA CCTAGTTTAG CCATTGCCCT 1430
GGAGATGAAA TTAATGGAGG CTCAAGGATA GATGAGCTCT GAGTTTCTCA GTACTCCCTC 1490
AAGACTGGAC ATCTTGGTCT TTTTCTCAGG CCTGAGGGGG AACCATTTTT GGTGTGATAA 1550
ATACCCTAAA CTGCCTTTTT TTCTTTTTTG AGGTGGGGGG AGGGAGGAGG TATATTGGAA 1610
CTCTTCTAAC CTCCTTGGGC TATATTTTCT CTCCTCGAGT TGCTCCTCAT GGCTGGGCTC 1670
ATTTCGGTCC CTTTCTCCTT GGTCCCAGAC CTTGGGGGAA AGGAAGGAAG TGCATGTTTG 1730
GGAACTGGCA TTACTGGAAC TAATGGTTTT AACCTCCTTA ACCACCAGCA TCCCTCCTCT 1790
CCCCAAGGTG AAGTGGAGGG TGCTGTGGTG AGCTGGCCAC TCCAGAGCTG CAGTGCCACT 1850
GGAGGAGTCA GACTACCATG ACATCGTAGG GAAGGAGGGG AGATTTTTTT GTAGTTTTTA 1910
ATTGGGGTGT GGGAGGGGCG GGGAGGTTTT CTATAAACTG TATCATTTTC TGCTGAGGGT 1970
GGAGTGTCCC ATCCTTTTAA TCAAGGTGAT TGTGATTTTG ACTAATAAAA AAGAATTTGT 2030

(2) INFORMATION FOR SEQ ID NO: 49:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 493
(B) TYPE: Nucleic acid
(C) STRANDEDNESS: Double
(D) TOPOLOGY: Linear
(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:
(A) ORGANISM: *Homo sapiens*
(B) CELL KIND: Stomach cancer
(D) CLONE NAME: HP10424

(ix) SEQUENCE CHARACTERISTICS:

(A) CHARACTERIZATION CODE: CDS

(B) EXISTENCE POSITION: 98.. 439

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:

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AAAGTTTCCC AAATCCAGGC GGCTAGAGGC CCACTGCTTC CCAACTACCA GCTGAGGGGG    60
TCCGTCCCGA GAAGGGAGAA GAGGCCGAAG AGGAAAC ATG AAC TTC TAT TTA CTC   115
                                         Met Asn Phe Tyr Leu Leu
                                          1               5
CTA GCG AGC AGC ATT CTG TGT GCC TTG ATT GTC TTC TGG AAA TAT CGC    163
Leu Ala Ser Ser Ile Leu Cys Ala Leu Ile Val Phe Trp Lys Tyr Arg
            10                  15                  20
CGC TTT CAG AGA AAC ACT GGC GAA ATG TCA TCA AAT TCA ACT GCT CTT    211
Arg Phe Gln Arg Asn Thr Gly Glu Met Ser Ser Asn Ser Thr Ala Leu
        25                  30                  35
GCA CTA GTG AGA CCC TCT TCT TCT GGG TTA ATT AAC AGC AAT ACA GAC    259
Ala Leu Val Arg Pro Ser Ser Ser Gly Leu Ile Asn Ser Asn Thr Asp
    40                  45                  50
AAC AAT CTT GCA GTC TAC GAC CTC TCT CGG GAT ATT TTA AAT AAT TTC    307
Asn Asn Leu Ala Val Tyr Asp Leu Ser Arg Asp Ile Leu Asn Asn Phe
 55                  60                  65                  70
CCA CAC TCA ATA GCC AGG CAG AAG CGA ATA TTG GTA AAC CTC AGT ATG    355
Pro His Ser Ile Ala Arg Gln Lys Arg Ile Leu Val Asn Leu Ser Met
                75                  80                  85
GTG GAA AAC AAG CTG GTT GAA CTG GAA CAT ACT CTA CTT AGC AAG GGT    403
Val Glu Asn Lys Leu Val Glu Leu Glu His Thr Leu Leu Ser Lys Gly
            90                  95                 100
TTC AGA GGT GCA TCA CCT CAC CGG AAA TCC ACC TAAAAGCGTA CAGG        450
Phe Arg Gly Ala Ser Pro His Arg Lys Ser Thr
        105                 110
ATGTAATGCC AGTGGTGGAA ATCATTAAAG ACACTTTGA GTAG                    493
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(2) INFORMATION FOR SEQ ID NO: 50:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2044

(B) TYPE: Nucleic acid
(C) STRANDEDNESS: Double
(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:
(A) ORGANISM: *Homo sapiens*
(B) CELL KIND: Epidermoid carcinoma
(C) CELL LINE: KB
(D) CLONE NAME: HP10428

(ix) SEQUENCE CHARACTERISTICS:
(A) CHARACTERIZATION CODE: CDS
(B) EXISTENCE POSITION: 288.. 1385
(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50:

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AGATTCCGGC CTGGAGCTCC CAGGGCCGAG CAGACCTTGG GACCTGTGAG CGCTGCATCC      60
AATTAACCAT GGGAAGGGTC AGCACCAGCC ACCAGCCCCT TAGGTGAGGA CTCTGCCTGG     120
GGCTCTGCTG ATGGTTCCGA ATCATGGAGC TGCAGAGAGC TCCTCCAGCC TGGAGACGTT     180
CTTGGTGAAA GCTGTGGTCT AACTCCACCG GCTCTTCCTG CACATTGTAT TCAAGAGGGG     240
TGCCTGCCCC CGCTGACTCA GGAGCTCCGG TGCTGCAGCC GCCACGA ATG GGG AGG       296
                                                    Met Gly Arg
                                                     1
TGG GCC CTC GAT GTG GCC TTT TTG TGG AAG GCG GTG TTG ACC CTG GGG       344
Trp Ala Leu Asp Val Ala Phe Leu Trp Lys Ala Val Leu Thr Leu Gly
     5                  10                  15
CTG GTG CTT CTC TAC TAC TGC TTC TCC ATC GGC ATC ACC TTC TAC AAC       392
Leu Val Leu Leu Tyr Tyr Cys Phe Ser Ile Gly Ile Thr Phe Tyr Asn
 20                  25                  30                  35
AAG TGG CTG ACA AAG AGC TTC CAT TTC CCC CTC TTC ATG ACG ATG CTG       440
Lys Trp Leu Thr Lys Ser Phe His Phe Pro Leu Phe Met Thr Met Leu
                 40                  45                  50
CAC CTG GCC GTG ATC TTC CTC TTC TCC GCC CTG TCC AGG GCG CTG GTT       488
His Leu Ala Val Ile Phe Leu Phe Ser Ala Leu Ser Arg Ala Leu Val
             55                  60                  65
CAG TGC TCC AGC CAC AGG GCC CGT GTG GTG CTG AGC TGG GCC GAC TAC       536
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Gln Cys Ser Ser His Arg Ala Arg Val Val Leu Ser Trp Ala Asp Tyr
          70                  75                  80
CTC AGA AGA GTG GCT CCC ACA GCT CTG GCG ACG GCG CTT GAC GTG GGC      584
Leu Arg Arg Val Ala Pro Thr Ala Leu Ala Thr Ala Leu Asp Val Gly
     85                  90                  95
TTG TCC AAC TGG AGC TTC CTG TAT GTC ACC GTC TCG CTG TAC ACA ATG      632
Leu Ser Asn Trp Ser Phe Leu Tyr Val Thr Val Ser Leu Tyr Thr Met
100                 105                 110                 115
ACC AAA TCC TCA GCT GTC CTC TTC ATC TTG ATC TTC TCT CTG ATC TTC      680
Thr Lys Ser Ser Ala Val Leu Phe Ile Leu Ile Phe Ser Leu Ile Phe
                120                 125                 130
AAG CTG GAG GAG CTG CGC GCG GCA CTG GTC CTG GTG GTC CTC CTC ATC      728
Lys Leu Glu Glu Leu Arg Ala Ala Leu Val Leu Val Val Leu Leu Ile
            135                 140                 145
GCC GGG GGT CTC TTC ATG TTC ACC TAC AAG TCC ACA CAG TTC AAC GTG      776
Ala Gly Gly Leu Phe Met Phe Thr Tyr Lys Ser Thr Gln Phe Asn Val
        150                 155                 160
GAG GGC TTC GCC TTG GTG CTG GGG GCC TCG TTC ATC GGT GGC ATT CGC      824
Glu Gly Phe Ala Leu Val Leu Gly Ala Ser Phe Ile Gly Gly Ile Arg
    165                 170                 175
TGG ACC CTC ACC CAG ATG CTC CTG CAG AAG GCT GAA CTC GGC CTC CAG      872
Trp Thr Leu Thr Gln Met Leu Leu Gln Lys Ala Glu Leu Gly Leu Gln
180                 185                 190                 195
AAT CCC ATC GAC ACC ATG TTC CAC CTG CAG CCA CTC ATG TTC CTG GGG      920
Asn Pro Ile Asp Thr Met Phe His Leu Gln Pro Leu Met Phe Leu Gly
                200                 205                 210
CTC TTC CCT CTC TTT GCT GTA TTT GAA GGT CTC CAT TTG TCC ACA TCT      968
Leu Phe Pro Leu Phe Ala Val Phe Glu Gly Leu His Leu Ser Thr Ser
            215                 220                 225
GAG AAA ATC TTC CGT TTC CAG GAC ACA GGG CTG CTC CTG CGG GTA CTT     1016
Glu Lys Ile Phe Arg Phe Gln Asp Thr Gly Leu Leu Leu Arg Val Leu
        230                 235                 240
GGG AGC CTC TTC CTT GGC GGG ATT CTC GCC TTT GGT TTG GGC TTC TCT     1064
Gly Ser Leu Phe Leu Gly Gly Ile Leu Ala Phe Gly Leu Gly Phe Ser
    245                 250                 255
GAG TTC CTC CTG GTC TCC AGA ACC TCC AGC CTC ACT CTC TCC ATT GCC     1112
Glu Phe Leu Leu Val Ser Arg Thr Ser Ser Leu Thr Leu Ser Ile Ala
260                 265                 270                 275
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GGC ATT TTT AAG GAA GTC TGC ACT TTG CTG TTG GCA GCT CAT CTG CTG      1160
Gly Ile Phe Lys Glu Val Cys Thr Leu Leu Leu Ala Ala His Leu Leu
                280                 285                 290
GGC GAT CAG ATC AGC CTC CTG AAC TGG CTG GGC TTC GCC CTC TGC CTC      1208
Gly Asp Gln Ile Ser Leu Leu Asn Trp Leu Gly Phe Ala Leu Cys Leu
            295                 300                 305
TCG GGA ATA TCC CTC CAC GTT GCC CTC AAA GCC CTG CAT TCC AGA GGT      1256
Ser Gly Ile Ser Leu His Val Ala Leu Lys Ala Leu His Ser Arg Gly
        310                 315                 320
GAT GGT GGC CCC AAG GCC TTG AAG GGG CTG GGC TCC AGC CCC GAC CTG      1304
Asp Gly Gly Pro Lys Ala Leu Lys Gly Leu Gly Ser Ser Pro Asp Leu
    325                 330                 335
GAG CTG CTG CTC CGG AGC AGC CAG CGG GAG GAA GGT GAC AAT GAG GAG      1352
Glu Leu Leu Leu Arg Ser Ser Gln Arg Glu Glu Gly Asp Asn Glu Glu
340                 345                 350                 355
GAG GAG TAC TTT GTG GCC CAG GGG CAG CAG TGACCAGCCA GGGCAAAT          1400
Glu Glu Tyr Phe Val Ala Gln Gly Gln Gln
                360                 365
GGCTTAGAAG CAGGCCACTC CCCAGCCTGC TGCCAGCACT CACTGTGCTC AAGCCGCCAG    1460
GGCTCATCAT GGTAGCTGGG AGCTGTGGAC GGGAGTCACC AGGTGGTGGG GCCAAGCCAG    1520
GGACTCATGA CTTTTGCCCC TCCCTTCAGA GCCTGGTCAC ACAAGGGGCG AGCACCAGGC    1580
CAGCCTGGGA CTGGCCAGAG CTGGGCCCAA GCTGCGCTGG AATCGCAGCA GGAGAGGGGA    1640
GTGGGCTGGT TCTTCCCACC ACTTCCCAGG CTCTGACAGC CGAGACTCAT TTCCAAGGCA    1700
CAGCAGCTTT CTAAAGGGAC TGAGTTTGGA CTGGGTTTTG GACCTCCAGG GGCTGGAGCT    1760
TCATCACCTG GGCAGTGTCT TTTCTCAGAG AGCAGGTTTC TTTATAGTTT GGAAATAAAT    1820
GGTTCACGGT CCACTGGCCG CCTTGTGTTG CTGGAGACGT GGGGGCAGGG AGGGGACAGT    1880
GTGGGCCTGG CCTCTCCTTT CCTTTCCCTG CCTGGAGCCT TCTTCAAATG TCTGGTCTTA    1940
AGCCAGGCCT CCTTCATTTT CTCGCTCCTG TTAGAACACC AGTCCCCTCC CCAGTGGGGC    2000
CCCACTGCAC CTGCTGGCAG GAAATAAATG AATGTTTACT GAGT                     2044
```

(2) INFORMATION FOR SEQ ID NO: 51:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1043

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10429

(ix) SEQUENCE CHARACTERISTICS:

(A) CHARACTERIZATION CODE: CDS

(B) EXISTENCE POSITION: 157.. 837

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:

```
ATTAGCATAA CCCTTCCTCA GGAAGAGTGA GATTTTATAT TTGACAATAA AGTGTTAGAC     60
TCCATTTCTA AATACCAGAC TTCAAAAGAT AAGGTTCAAA AGTGTTATAA GAAGATATTC    120
CTTTTTTTGT CCTAGAGAAC TTATTTTCCT GTGAAA ATG CCT ACC ACA AAG AAG      174
                                        Met Pro Thr Thr Lys Lys
                                         1               5
ACA TTG ATG TTC TTA TCA AGC TTT TTC ACC AGC CTT GGG TCC TTC ATT      222
Thr Leu Met Phe Leu Ser Ser Phe Phe Thr Ser Leu Gly Ser Phe Ile
             10                  15                  20
GTA ATT TGC TCT ATT CTT GGG ACA CAA GCA TGG ATC ACC AGT ACA ATT      270
Val Ile Cys Ser Ile Leu Gly Thr Gln Ala Trp Ile Thr Ser Thr Ile
         25                  30                  35
GCT GTT AGA GAC TCT GCT TCA AAT GGG AGC ATT TTC ATC ACT TAC GGA      318
Ala Val Arg Asp Ser Ala Ser Asn Gly Ser Ile Phe Ile Thr Tyr Gly
     40                  45                  50
CTT TTT CGT GGG GAG AGT AGT GAA GAA TTG AGT CAC GGA CTT GCA GAA      366
Leu Phe Arg Gly Glu Ser Ser Glu Glu Leu Ser His Gly Leu Ala Glu
 55                  60                  65                  70
CCA AAG AAA AAG TTT GCA GTT TTA GAG ATA CTG AAT AAT TCT TCC CAA      414
Pro Lys Lys Lys Phe Ala Val Leu Glu Ile Leu Asn Asn Ser Ser Gln
                 75                  80                  85
AAA ACT CTG CAT TCG GTG ACT ATC CTG TTC CTG GTC CTG AGT TTG ATC      462
Lys Thr Leu His Ser Val Thr Ile Leu Phe Leu Val Leu Ser Leu Ile
             90                  95                 100
ACG TCG CTG CTG AGC TCT GGG TTT ACC TTC TAC AAC AGC ATC AGC AAC      510
Thr Ser Leu Leu Ser Ser Gly Phe Thr Phe Tyr Asn Ser Ile Ser Asn
        105                 110                 115
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CCT TAC CAG ACA TTC CTG GGG CCG ACG GGG GTG TAC ACC TGG AAC GGG      558
Pro Tyr Gln Thr Phe Leu Gly Pro Thr Gly Val Tyr Thr Trp Asn Gly
    120                 125                 130
CTC GGT GCA TCC TTC GTT TTT GTG ACC ATG ATA CTG TTT GTG GCG AAC      606
Leu Gly Ala Ser Phe Val Phe Val Thr Met Ile Leu Phe Val Ala Asn
135                 140                 145                 150
ACG CAG TCC AAC CAA CTC TCC GAA GAG TTG TTC CAA ATG CTT TAC CCG      654
Thr Gln Ser Asn Gln Leu Ser Glu Glu Leu Phe Gln Met Leu Tyr Pro
                155                 160                 165
GCA ACC ACC AGT AAA GGA ACG ACC CAC AGT TAC GGA TAC TCG TTC TGG      702
Ala Thr Thr Ser Lys Gly Thr Thr His Ser Tyr Gly Tyr Ser Phe Trp
            170                 175                 180
CTC ATA CTG CTC GTC ATT CTT CTA AAT ATA GTC ACT GTA ACC ATC ATC      750
Leu Ile Leu Leu Val Ile Leu Leu Asn Ile Val Thr Val Thr Ile Ile
        185                 190                 195
ATT TTC TAC CAG AAG GCC AGA TAC CAG CGG AAG CAG GAG CAG AGA AAG      798
Ile Phe Tyr Gln Lys Ala Arg Tyr Gln Arg Lys Gln Glu Gln Arg Lys
    200                 205                 210
CCA ATG GAA TAT GCT CCA AGG GAC GGA ATT TTA TTC TGAATTCTCT TTCATC    850
Pro Met Glu Tyr Ala Pro Arg Asp Gly Ile Leu Phe
215                 220                 225
TCATTTTGGC GTTGCATCTA TTGTACATCA GCCCTGAGTA GTAACTGGTT AGCTTCTCTG    910
GACAATTCAG CATGGTAACG TGACTGTCAT CTGTGACAGC ATTTGTGTTT CATGACACTG    970
TGTTCTTCAT TGATGCTGTA CTCCTGAAAA TTTTTCCCAC AAGGTTGGGG AAATGAATGG   1030
GAAATGTCGC TGG                                                      1043
```

(2) INFORMATION FOR SEQ ID NO: 52:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 972

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Liver

(D) CLONE NAME: HP10432

(ix) SEQUENCE CHARACTERISTICS:
(A) CHARACTERIZATION CODE: CDS
(B) EXISTENCE POSITION: 29.. 418
(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

```
AGACAGCGGC GGGCGCAGGA CGTGCACT ATG GCT CGG GGC TCG CTG CGC CGG        52
                                   Met Ala Arg Gly Ser Leu Arg Arg
                                    1               5
TTG CTG CGG CTC CTC GTG CTG GGG CTC TGG CTG GCG TTG CTG CGC TCC      100
Leu Leu Arg Leu Leu Val Leu Gly Leu Trp Leu Ala Leu Leu Arg Ser
     10                  15                  20
GTG GCC GGG GAG CAA GCG CCA GGC ACC GCC CCC TGC TCC CGC GGC AGC      148
Val Ala Gly Glu Gln Ala Pro Gly Thr Ala Pro Cys Ser Arg Gly Ser
 25                  30                  35                  40
TCC TGG AGC GCG GAC CTG GAC AAG TGC ATG GAC TGC GCG TCT TGC AGG      196
Ser Trp Ser Ala Asp Leu Asp Lys Cys Met Asp Cys Ala Ser Cys Arg
                 45                  50                  55
GCG CGA CCG CAC AGC GAC TTC TGC CTG GGC TGC GCT GCA GCA CCT CCT      244
Ala Arg Pro His Ser Asp Phe Cys Leu Gly Cys Ala Ala Ala Pro Pro
             60                  65                  70
GCC CCC TTC CGG CTG CTT TGG CCC ATC CTT GGG GGC GCT CTG AGC CTG      292
Ala Pro Phe Arg Leu Leu Trp Pro Ile Leu Gly Gly Ala Leu Ser Leu
         75                  80                  85
ACC TTC GTG CTG GGG CTG CTT TCT GGC TTT TTG GTC TGG AGA CGA TGC      340
Thr Phe Val Leu Gly Leu Leu Ser Gly Phe Leu Val Trp Arg Arg Cys
     90                  95                  100
CGC AGG AGA GAG AAG TTC ACC ACC CCC ATA GAG GAG ACC GGC GGA GAG      388
Arg Arg Arg Glu Lys Phe Thr Thr Pro Ile Glu Glu Thr Gly Gly Glu
105                 110                 115                 120
GGC TGC CCA GCT GTG GCG CTG ATC CAG TGACA ATGT GCCCCCTGCC A CCGG      440
Gly Cys Pro Ala Val Ala Leu Ile Gln
                125
GGCTCGCCCA CTCATCATTC ATTCATCCAT TCTAGAGCCA GTCTCTGCCT CCCAGACGCG     500
GCGGGAGCCA AGCTCCTCCA ACCACAAGGG GGGTGGGGGG CGGTGAATCA CCTCTGAGGC     560
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CTGGGCCCAG GGTTCAGGGG AACCTTCCAA GGTGTCTGGT TGCCCTGCCT CTGGCTCCAG     620
AACAGAAAGG GAGCCTCACG CTGGCTCACA CAAAACAGCT GACACTGACT AAGGAACTGC     680
AGCATTTGCA CAGGGGAGGG GGGTGCCCTC CTTCCTAGAG GCCCTGGGGG CCAGGCTGAC     740
TTGGGGGGCA GACTTGACAC TAGGCCCCAC TCACTCAGAT GTCCTGAAAT TCCACCACGG     800
GGGTCACCCT GGGGGGTTAG GGACCTATTT TTAACACTAG GGGGCTGGCC CACTAGGAGG     860
GCTGGCCCTA AGATACAGAC CCCCCCAACT CCCCAAAGCG GGGAGGAGAT ATTTATTTTG     920
GGGAGAGTTT GGAGGGGAGG GAGAATTTAT TAATAAAAGA ATCTTTAACT TT             972
```

(2) INFORMATION FOR SEQ ID NO: 53:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 695

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: *Homo sapiens*

(B) CELL KIND: Liver

(C) CELL LINE:

(D) CLONE NAME: HP10433

(ix) SEQUENCE CHARACTERISTICS:

(A) CHARACTERIZATION CODE: CDS

(B) EXISTENCE POSITION: 73.. 564

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

```
AAGATTTCAG CTGCGGGACG GTCAGGGGAG ACCTCCAGGC GCAGGGAAGG ACGGCCAGGG      60
TGACACGGAA GC ATG CGA CGG CTG CTG ATC CCT CTG GCC CTG TGG CTG GGC     111
              Met Arg Arg Leu Leu Ile Pro Leu Ala Leu Trp Leu Gly
                1               5                  10
GCG GTG GGC GTG GGC GTC GCC GAG CTC ACG GAA GCC CAG CGC CGG GGC      159
Ala Val Gly Val Gly Val Ala Glu Leu Thr Glu Ala Gln Arg Arg Gly
     15                  20                  25
CTG CAG GTG GCC CTG GAG GAA TTT CAC AAG CAC CCG CCC GTG CAG TGG      207
```

Leu Gln Val Ala Leu Glu Glu Phe His Lys His Pro Pro Val Gln Trp
30 35 40 45
GCC TTC CAG GAG ACC AGT GTG GAG AGC GCC GTG GAC ACG CCC TTC CCA 255
Ala Phe Gln Glu Thr Ser Val Glu Ser Ala Val Asp Thr Pro Phe Pro
50 55 60
GCT GGA ATA TTT GTG AGG CTG GAA TTT AAG CTG CAG CAG ACA AGC TGC 303
Ala Gly Ile Phe Val Arg Leu Glu Phe Lys Leu Gln Gln Thr Ser Cys
65 70 75
CGG AAG AGG GAC TGG AAG AAA CCC GAG TGC AAA GTC AGG CCC AAT GGG 351
Arg Lys Arg Asp Trp Lys Lys Pro Glu Cys Lys Val Arg Pro Asn Gly
80 85 90
AGG AAA CGG AAA TGC CTG GCC TGC ATC AAA CTG GGC TCT GAG GAC AAA 399
Arg Lys Arg Lys Cys Leu Ala Cys Ile Lys Leu Gly Ser Glu Asp Lys
95 100 105
GTT CTG GGC CGG TTG GTC CAC TGC CCC ATA GAG ACC CAA GTT CTG CGG 447
Val Leu Gly Arg Leu Val His Cys Pro Ile Glu Thr Gln Val Leu Arg
110 115 120 125
GAG GCT GAG GAG CAC CAG GAG ACC CAG TGC CTC AGG GTG CAG CGG GCT 495
Glu Ala Glu Glu His Gln Glu Thr Gln Cys Leu Arg Val Gln Arg Ala
130 135 140
GGT GAG GAC CCC CAC AGC TTC TAC TTC CCT GGA CAG TTC GCC TTC TCC 543
Gly Glu Asp Pro His Ser Phe Tyr Phe Pro Gly Gln Phe Ala Phe Ser
145 150 155
AAG GCC CTG CCC CGC AGC TAAGCCAGCA CTGAGCTGCG TGGTGCCTC 590
Lys Ala Leu Pro Arg Ser
160
CAGGACCGCT GCCGGTGGTA ACCAGTGGAA GACCCCAGCC CCCAGGGAGA GGACCCCGTT 650
CTATCCCCAG CCATGATAAT AAAGCTGCTC TCCCAGCTGC CTCTC 695

(2) INFORMATION FOR SEQ ID NO: 54:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1914

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:
(A) ORGANISM: *Homo sapiens*
(B) CELL KIND: Stomach cancer
(D) CLONE NAME: HP10480

(ix) SEQUENCE CHARACTERISTICS:
(A) CHARACTERIZATION CODE: CDS
(B) EXISTENCE POSITION: 80.. 661
(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:

```
ACTCTCTGCT GTCGCCCGTC CCGCGCGCTC CTCCGACCCG CTCCGCTCCG CTCCGCTCGG      60
CCCCGCGCCG CCCGTCAAC ATG ATC CGC TGC GGC CTG GCC TGC GAG CGC TGC      112
                     Met Ile Arg Cys Gly Leu Ala Cys Glu Arg Cys
                       1               5                  10
CGC TGG ATC CTG CCC CTG CTC CTA CTC AGC GCC ATC GCC TTC GAC ATC      160
Arg Trp Ile Leu Pro Leu Leu Leu Leu Ser Ala Ile Ala Phe Asp Ile
                  15                  20                  25
ATC GCG CTG GCC GGC CGC GGC TGG TTG CAG TCT AGC GAC CAC GGC CAG      208
Ile Ala Leu Ala Gly Arg Gly Trp Leu Gln Ser Ser Asp His Gly Gln
          30                  35                  40
ACG TCC TCG CTG TGG TGG AAA TGC TCC CAA GAG GGC GGC GGC AGC GGG      256
Thr Ser Ser Leu Trp Trp Lys Cys Ser Gln Glu Gly Gly Gly Ser Gly
      45                  50                  55
TCC TAC GAG GAG GGC TGT CAG AGC CTC ATG GAG TAC GCG TGG GGT AGA      304
Ser Tyr Glu Glu Gly Cys Gln Ser Leu Met Glu Tyr Ala Trp Gly Arg
 60                  65                  70                  75
GCA GCG GCT GCC ATG CTC TTC TGT GGC TTC ATC ATC CTG GTG ATC TGT      352
Ala Ala Ala Ala Met Leu Phe Cys Gly Phe Ile Ile Leu Val Ile Cys
                  80                  85                  90
TTC ATC CTC TCC TTC TTC GCC CTC TGT GGA CCC CAG ATG CTT GTC TTC      400
Phe Ile Leu Ser Phe Phe Ala Leu Cys Gly Pro Gln Met Leu Val Phe
              95                  100                 105
CTG AGA GTG ATT GGA GGT CTC CTT GCC TTG GCT GCT GTG TTC CAG ATC      448
Leu Arg Val Ile Gly Gly Leu Leu Ala Leu Ala Ala Val Phe Gln Ile
          110                 115                 120
ATC TCC CTG GTA ATT TAC CCC GTG AAG TAC ACC CAG ACC TTC ACC CTT      496
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Ile Ser Leu Val Ile Tyr Pro Val Lys Tyr Thr Gln Thr Phe Thr Leu
    125                 130                 135
CAT GCC AAC CGT GCT GTC ACT TAC ATC TAT AAC TGG GCC TAC GGC TTT      544
His Ala Asn Arg Ala Val Thr Tyr Ile Tyr Asn Trp Ala Tyr Gly Phe
140                 145                 150                 155
GGG TGG GCA GCC ACG ATT ATC CTG ATC GGC TGT GCC TTC TTC TTC TGC      592
Gly Trp Ala Ala Thr Ile Ile Leu Ile Gly Cys Ala Phe Phe Phe Cys
                160                 165                 170
TGC CTC CCC AAC TAC GAA GAT GAC CTT CTG GGC AAT GCC AAG CCC AGG      640
Cys Leu Pro Asn Tyr Glu Asp Asp Leu Leu Gly Asn Ala Lys Pro Arg
            175                 180                 185
TAC TTC TAC ACA TCT GCC TA ACTTGGG AATGAATGTG GGAGAAAATC GCT         690
Tyr Phe Tyr Thr Ser Ala
        190
GCTGCTGAGA TGGACTCCAG AAGAAGAAAC TGTTTCTCCA GGCGACTTTG AACCCATTTT    750
TTGGCAGTGT TCATATTATT AAACTAGTCA AAAATGCTAA AATAATTTGG GAGAAAATAT    810
TTTTTAAGTA GTGTTATAGT TTCATGTTTA TCTTTTATTA TGTTTTGTGA AGTTGTGTCT    870
TTTCACTAAT TACCTATACT ATGCCAATAT TTCCTTATAT CTATCCATAA CATTTATACT    930
ACATTTGTAA GAGAATATGC ACGTGAAACT TAACACTTTA TAAGGTAAAA ATGAGGTTTC    990
CAAGATTTAA TAATCTGATC AAGTTCTTGT TATTTCCAAA TAGAATGGAC TTGGTCTGTT   1050
AAGGGCTAAG GAGAAGAGGA AGATAAGGTT AAAAGTTGTT AATGACCAAA CATTCTAAAA   1110
GAAATGCAAA AAAAAAGTTT ATTTTCAAGC CTTCGAACTA TTTAAGGAAA GCAAAATCAT   1170
TTCCTAAATG CATATCATTT GTGAGAATTT CTCATTAATA TCCTGAATCA TTCATTTCAG   1230
CTAAGGCTTC ATGTTGACTC GATATGTCAT CTAGGAAAGT ACTATTTCAT GGTCCAAACC   1290
TGTTGCCATA GTTGGTAAGG CTTTCCTTTA AGTGTGAAAT ATTTAGATGA AATTTTCTCT   1350
TTTAAAGTTC TTTATAGGGT TAGGGTGTGG GAAAATGCTA TATTAATAAA TCTGTAGTGT   1410
TTTGTGTTTA TATGTTCAGA ACCAGAGTAG ACTGGATTGA AAGATGGACT GGGTCTAATT   1470
TATCATGACT GATAGATCTG GTTAAGTTGT GTAGTAAAGC ATTAGGAGGG TCATTCTTGT   1530
CACAAAAGTG CCACTAAAAC AGCCTCAGGA GAATAAATGA CTTGCTTTTC TAAATCTCAG   1590
GTTTATCTGG GCTCTATCAT ATAGACAGGC TTCTGATAGT TTGCAACTGT AAGCAGAAAC   1650
CTACATATAG TTAAAATCCT GGTCTTTCTT GGTAAACAGA TTTTAAATGT CTGATATAAA   1710
ACATGCCACA GGAGAATTCG GGGATTTGAG TTTCTCTGAA TAGCATATAT ATGATGCATC   1770
GGATAGGTCA TTATGATTTT TTACCATTTC GACTTACATA ATGAAAACCA ATTCATTTTA   1830
AATATCAGAT TATTATTTTG TAAGTTGTGG AAAAAGCTAA TTGTAGTTTT CATTATGAAG   1890
TTTTCCCAAT AAACCAGGTA TTCT                                          1914
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PATENT COOPERATION TREATY

REC'D 20 SEP 1999
WIPO PCT

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
660479		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP98/02445	03/06/1998	03/06/1997

International Patent Classification (IPC) or national classification and IPC
C12N15/12

Applicant
SAGAMI CHEMICAL RESEARCH CENTER et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report
   II ☐ Priority
   III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   IV ☒ Lack of unity of invention
   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   VI ☐ Certain documents cited
   VII ☐ Certain defects in the international application
   VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17/12/1998	14.09.99
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Kaas, V Telephone No. +49 89 2399 8704

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP98/02445

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-156 as originally filed

Claims, No.:

1-6 as originally filed

Drawings, sheets:

1/19-19/19 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-6 (all partially).

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-6 (all partially).

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-6 (all partially).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-6
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-6
Industrial applicability (IA)	Yes:	Claims	1-6
	No:	Claims	

2. Citations and explanations

see separate sheet

1) For the reasons given in the International Preliminary Search Report, the application is considered to lack unity of invention (Rule 13 PCT). Given that no reuired additional seearch fees were timely paid by the applicant, the present IPER is limited to invention 1 (Claims 1-6, all partially) as mentioned therein.

2) Claims 1-4 relate to a cDNA clone (SEQ ID NO: 19 and 37) identified with the help of automated processing from a human liver cDNA library and to the polypeptide (SEQ ID NO: 1) allegedly expressed by said clone. However, the application fails to provide any evidence that the clone is capable of expressing a protein which is functional. In this respect, the mere fact that a protein appears to display a hydrophobic region of putative transmembrane domain(s) is not considered to represent such evidence. Moreover, there appears to be no substantial support therein for any of the numerous alleged putative technical useful properties which are merely listed in the description on pages 56 to 82. The present application is therefore considered to provide a human cDNA sequence encoding a polypeptide with no identified biological properties.

In this case, any prior art coumpound, regardless of its technical properties, is equally suitable as the starting point for making structural modifications and may be considred to represent the closest prior art.

Starting from this point, the objective technical problem to be solved can thus be formulated to lie in the provision of further human cDNA sequences as such, regardless of their possible useful properties. Without the concommitant need to provide any particular technical effect, the skilled person would have the choice of an infinite number of equally obvious possible solutions. In this respect, any DNA sequence of a human cDNA library is considered to obviously solve the above problem. The claimed polynucleotide molecule therefore represents the result of an arbitrary selection among the cDNA clones which can be routinely isolated from a human cDNA library, e.g. identified by quering an EST database for sequences possessing a putative secretion signal. Such an arbitrary selection cannot involve an inventive step because it is not justified by any technical purpose related to an hitherto unknown or unexpected technical effect resulting from those structural features which distinguish the compound claimed from all other possibilities.

Thus, for nucleotide and peptide sequences whose function and, in the latter case, existance is based purely upon surmise, inventive step cannot be acknowledged.

Claims 1-4 therefore do not satisfy the criterions as set forth in Article 33(3) PCT.

3) The preparation of a conventional expression vector comprising portions of the nucleotide sequence as well as the transformation of an eucaryotic cell with said vector do not appear to go beyond the knowledge and capabilities of the skilled person. Claims 5 and 6 therefore also lack inventiveness.

4) Claims 1-6 of invention 1 appear to be susceptible of industrial applicability as defined in Article 33(4) PCT.

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

United States Patent and Trademark Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 28 January 1999 (28.01.99)	
International application No. PCT/JP98/02445	**Applicant's or agent's file reference** 660479
International filing date (day/month/year) 03 June 1998 (03.06.98)	**Priority date** (day/month/year) 03 June 1997 (03.06.97)
Applicant KATO, Seishi et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

17 December 1998 (17.12.98)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer K. Takeda
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
660479		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/JP 98/ 02445	03/06/1998	03/06/1997
Applicant		
SAGAMI CHEMICAL RESEARCH CENTER et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ **Certain claims were found unsearchable** (see Box I).

2. ☒ **Unity of invention is lacking** (see Box II).

3. ☒ The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
   - ☒ filed with the international application.
   - ☐ furnished by the applicant separately from the international application,
     - ☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
   - ☐ Transcribed by this Authority

4. With regard to the **title,**
   - ☒ the text is approved as submitted by the applicant.
   - ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   - ☒ the text is approved as submitted by the applicant.
   - ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:
   Figure No. _____
   - ☐ as suggested by the applicant.
   - ☐ because the applicant failed to suggest a figure.
   - ☐ because this figure better characterizes the invention.
   - ☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/JP 98/02445

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C07K14/705 A61K38/17 C12N5/10 C12Q1/37
C12N9/72 C12N15/85

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KYTE J. ET AL.: "A SIMPLE METHOD FOR DISPLAYING THE HYDROPATHIC CHARACTER OF A PROTEIN" JOURNAL OF MOLECULAR BIOLOGY, vol. 157, no. 1, 5 May 1982, pages 105-132, XP000609692 cited in the application ---	
A	LIBERT F. ET AL.: "SELECTIVE AMPLIFICATION AND CLONING OF FOUR NEW MEMBERS OF THE G PROTEIN-COUPLED RECEPTOR FAMILY" SCIENCE, vol. 244, 5 May 1989, pages 569-572, XP002041588 --- -/--	

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 September 1998	26. 01. 99

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Macchia, G

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MILLS A. AND DUGGAN M.J.: "ORPHAN SEVEN TRANSMEMBRANE DOMAIN RECEPTORS: REVERSING PHARMACOLOGY" TRENDS IN BIOTECHNOLOGY, vol. 12, February 1994, pages 47-49, XP002078287 ---	
A	Database EMBL, entry Emest7:HS010272 Accession number N39010 25 January 1996 99% identity with Seq.ID:19 nt.647-1146. XP002078288 see the whole document ---	2-4
A	Database EMBL, entry Emest9:HS204207 Accession number H57204 7 October 1995 96% identity with Seq.ID:19 nt.1-437. XP002078292 cited in the application see the whole document -----	2-4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP 98/02445

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-6 : all partially (see subject 1, extra sheet)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-6 all partially.

   A protein comprising an aminoacid sequence as in Seq.ID:1, encoding DNA, as in Seq.ID19 and 37, related expression vector and transformed eukaryotic cell.

2. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:2, 20 and 38.

3. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:3, 21 and 39.

4. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:4, 22 and 40.

5. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:5, 23 and 41.

6. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:6, 24 and 42.

7. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:7, 25 and 43.

8. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:8, 26 and 44.

9. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:9, 27 and 45.

10. Claims: 1-6 all partially.

    As invention 1 but concerning Seq.ID:10, 28 and 46.

11. Claims: 1-6 all partially.

    As invention 1 but concerning Seq.ID:11, 29 and 47.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

12. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:12, 30 and 48.

13. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:13, 31 and 49.

14. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:14, 32 and 50.

15. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:15, 33 and 51.

16. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:16, 34 and 52.

17. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:17, 35 and 53.

18. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:18, 36 and 54.

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

AOYAMA, Tamotsu
Aoyama & Partners
IMP Building
3-7, Shiromi 1-chome
Chuo-ku, Osaka-shi
Osaka 540-0001
JAPON

Date of mailing (day/month/year)
29 March 1999 (29.03.99)

Applicant's or agent's file reference
660479

IMPORTANT NOTIFICATION

International application No.
PCT/JP98/02445

International filing date (day/month/year)
03 June 1998 (03.06.98)

1. The following indications appeared on record concerning:

[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address
YAMAGUCHI, Tomoko
5-13-11, Takasago
Katsushika-ku
Tokyo 125
Japan

State of Nationality: JP
State of Residence: JP
Telephone No.:
Facsimile No.:
Teleprinter No.:

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [X] the name [X] the address [ ] the nationality [ ] the residence

Name and Address
KIMURA, Tomoko
302, 4-1-28, Nishiikuta
Tama-ku
Kawasaki-shi
Kanagawa 214-0037
Japan

State of Nationality: JP
State of Residence: JP
Telephone No.:
Facsimile No.:
Teleprinter No.:

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[X] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer
K. Takeda

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

AOYAMA, Tamotsu et al
Aoyama & Partners
IMP Building, 3-7 Shiromi 1-chome
Chuo-ku, Osaka-shi
Osaka 540
JAPON

受付
11.9.20
青山特許事務所

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	14.09.99
Applicant's or agent's file reference 660479	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP98/02445	03/06/1998	03/06/1997

Applicant
SAGAMI CHEMICAL RESEARCH CENTER et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Express Mail mailing label number EL [illegible]
Date of Deposit December 1, 1999
I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner For Patents, Washington, D.C. 20231
[signature]

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Vullo, C Tel.+49 89 2399-8061

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
660479		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP98/02445	03/06/1998	03/06/1997

International Patent Classification (IPC) or national classification and IPC
C12N15/12

Applicant
SAGAMI CHEMICAL RESEARCH CENTER et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report
   II ☐ Priority
   III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   IV ☒ Lack of unity of invention
   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   VI ☐ Certain documents cited
   VII ☐ Certain defects in the international application
   VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17/12/1998	14.09.99
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Kaas, V Telephone No. +49 89 2399 8704

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP98/02445

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-156 as originally filed

Claims, No.:

1-6 as originally filed

Drawings, sheets:

1/19-19/19 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-6 (all partially).

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-6 (all partially).

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1,.13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-6 (all partially).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-6
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-6
Industrial applicability (IA)	Yes:	Claims	1-6
	No:	Claims	

2. Citations and explanations

see separate sheet

1) For the reasons given in the International Preliminary Search Report, the application is considered to lack unity of invention (Rule 13 PCT). Given that no reuired additional seearch fees were timely paid by the applicant, the present IPER is limited to invention 1 (Claims 1-6, all partially) as mentioned therein.

2) Claims 1-4 relate to a cDNA clone (SEQ ID NO: 19 and 37) identified with the help of automated processing from a human liver cDNA library and to the polypeptide (SEQ ID NO: 1) allegedly expressed by said clone. However, the application fails to provide any evidence that the clone is capable of expressing a protein which is functional. In this respect, the mere fact that a protein appears to display a hydrophobic region of putative transmembrane domain(s) is not considered to represent such evidence. Moreover, there appears to be no substantial support therein for any of the numerous alleged putative technical useful properties which are merely listed in the description on pages 56 to 82. The present application is therefore considered to provide a human cDNA sequence encoding a polypeptide with no identified biological properties.

In this case, any prior art coumpound, regardless of its technical properties, is equally suitable as the starting point for making structural modifications and may be considred to represent the closest prior art.

Starting from this point, the objective technical problem to be solved can thus be formulated to lie in the provision of further human cDNA sequences as such, regardless of their possible useful properties. Without the concommitant need to provide any particular technical effect, the skilled person would have the choice of an infinite number of equally obvious possible solutions. In this respect, any DNA sequence of a human cDNA library is considered to obviously solve the above problem. The claimed polynucleotide molecule therefore represents the result of an arbitrary selection among the cDNA clones which can be routinely isolated from a human cDNA library, e.g. identified by quering an EST database for sequences possessing a putative secretion signal. Such an arbitrary selection cannot involve an inventive step because it is not justified by any technical purpose related to an hitherto unknown or unexpected technical effect resulting from those structural features which distinguish the compound claimed from all other possibilities.

Thus, for nucleotide and peptide sequences whose function and, in the latter case, existance is based purely upon surmise, inventive step cannot be acknowledged.

Claims 1-4 therefore do not satisfy the criterions as set forth in Article 33(3) PCT.

3) The preparation of a conventional expression vector comprising portions of the nucleotide sequence as well as the transformation of an eucaryotic cell with said vector do not appear to go beyond the knowledge and capabilities of the skilled person. Claims 5 and 6 therefore also lack inventiveness.

4) Claims 1-6 of invention 1 appear to be susceptible of industrial applicability as defined in Article 33(4) PCT.

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

受付
11. 2. 1
特許事務所

To:
Aoyama & Partners
IMP Building, 3-7 Shiromi 1-chome
Chuo-ku, Osaka-shi
Osaka 540
JAPAN

	Date of mailing (*day/month/year*) 26/01/1999
Applicant's or agent's file reference 660479	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/JP 98/02445	International filing date (*day/month/year*) 03/06/1998
Applicant SAGAMI CHEMICAL RESEARCH CENTER et al.	

"Express Mail" mailing label number EE632204666US
Date of Deposit December 1, 1999
I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1 10 on the date indicated above and is addressed to the Assistant Commissioner For Patents, Washington, D.C. 20231

1. [X] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   [ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicants's request to forward the texts of both the protest and the decision thereon to the designated Offices.

   [ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Andria Overbeeke-Siepkes

Form PCT/ISA/220 (January 1994)

外国方式

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to theprovisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international pbulication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been /is filed, see below.

How? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped),whether

(i) the claim is unchanged;

(ii) the claim is cancelled;

(iii) the claim is new;

(iv) the claim replaces one or more claims as filed;

(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."

2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."

3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."

4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
660479		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/JP 98/02445	03/06/1998	03/06/1997
Applicant		
SAGAMI CHEMICAL RESEARCH CENTER et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ **Certain claims were found unsearchable** (see Box I).

2. ☒ **Unity of invention is lacking** (see Box II).

3. ☒ The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
   - ☒ filed with the international application.
   - ☐ furnished by the applicant separately from the international application,
     - ☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
   - ☐ Transcribed by this Authority

4. With regard to the **title,**
   - ☒ the text is approved as submitted by the applicant.
   - ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   - ☒ the text is approved as submitted by the applicant.
   - ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:
   Figure No. _____
   - ☐ as suggested by the applicant.
   - ☐ because the applicant failed to suggest a figure.
   - ☐ because this figure better characterizes the invention.
   - ☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/JP 98/02445

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C07K14/705 A61K38/17 C12N5/10 C12Q1/37
C12N9/72 C12N15/85

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KYTE J. ET AL.: "A SIMPLE METHOD FOR DISPLAYING THE HYDROPATHIC CHARACTER OF A PROTEIN" JOURNAL OF MOLECULAR BIOLOGY, vol. 157, no. 1, 5 May 1982, pages 105-132, XP000609692 cited in the application ---	
A	LIBERT F. ET AL.: "SELECTIVE AMPLIFICATION AND CLONING OF FOUR NEW MEMBERS OF THE G PROTEIN-COUPLED RECEPTOR FAMILY" SCIENCE, vol. 244, 5 May 1989, pages 569-572, XP002041588 --- -/--	

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 September 1998	26. 01. 99

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Macchia, G

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MILLS A. AND DUGGAN M.J.: "ORPHAN SEVEN TRANSMEMBRANE DOMAIN RECEPTORS: REVERSING PHARMACOLOGY" TRENDS IN BIOTECHNOLOGY, vol. 12, February 1994, pages 47-49, XP002078287 ---	
A	Database EMBL, entry Emest7:HS010272 Accession number N39010 25 January 1996 99% identity with Seq.ID:19 nt.647-1146. XP002078288 see the whole document ---	2-4
A	Database EMBL, entry Emest9:HS204207 Accession number H57204 7 October 1995 96% identity with Seq.ID:19 nt.1-437. XP002078292 cited in the application see the whole document -----	2-4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP 98/02445

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-6 : all partially (see subject 1, extra sheet)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-6 all partially.

   A protein comprising an aminoacid sequence as in Seq.ID:1, encoding DNA, as in Seq.ID19 and 37, related expression vector and transformed eukaryotic cell.

2. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:2, 20 and 38.

3. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:3, 21 and 39.

4. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:4, 22 and 40.

5. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:5, 23 and 41.

6. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:6, 24 and 42.

7. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:7, 25 and 43.

8. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:8, 26 and 44.

9. Claims: 1-6 all partially.

   As invention 1 but concerning Seq.ID:9, 27 and 45.

10. Claims: 1-6 all partially.

    As invention 1 but concerning Seq.ID:10, 28 and 46.

11. Claims: 1-6 all partially.

    As invention 1 but concerning Seq.ID:11, 29 and 47.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

12. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:12, 30 and 48.

13. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:13, 31 and 49.

14. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:14, 32 and 50.

15. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:15, 33 and 51.

16. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:16, 34 and 52.

17. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:17, 35 and 53.

18. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:18, 36 and 54.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
660479		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/JP 98/02445	03/06/1998	03/06/1997
Applicant		
SAGAMI CHEMICAL RESEARCH CENTER et al.		

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This International Search Report consists of a total of 6 sheets.

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   - ☐ furnished by the applicant separately from the international application,
     - ☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
   - ☐ Transcribed by this Authority

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   - ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
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   - ☐ as suggested by the applicant.
   - ☐ because the applicant failed to suggest a figure.
   - ☐ because this figure better characterizes the invention.
   - ☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/JP 98/02445

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/12 C07K14/705 A61K38/17 C12N5/10 C12Q1/37
C12N9/72 C12N15/85

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 September 1998	26. 01. 99

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Macchia, G

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MILLS A. AND DUGGAN M.J.: "ORPHAN SEVEN TRANSMEMBRANE DOMAIN RECEPTORS: REVERSING PHARMACOLOGY" TRENDS IN BIOTECHNOLOGY, vol. 12, February 1994, pages 47-49, XP002078287 ---	
A	Database EMBL, entry Emest7:HS010272 Accession number N39010 25 January 1996 99% identity with Seq.ID:19 nt.647-1146. XP002078288 see the whole document ---	2-4
A	Database EMBL, entry Emest9:HS204207 Accession number H57204 7 October 1995 96% identity with Seq.ID:19 nt.1-437. XP002078292 cited in the application see the whole document -----	2-4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP 98/02445

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-6 : all partially (see subject 1, extra sheet)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-6 all partially.

A protein comprising an aminoacid sequence as in Seq.ID:1, encoding DNA, as in Seq.ID19 and 37, related expression vector and transformed eukaryotic cell.

2. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:2, 20 and 38.

3. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:3, 21 and 39.

4. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:4, 22 and 40.

5. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:5, 23 and 41.

6. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:6, 24 and 42.

7. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:7, 25 and 43.

8. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:8, 26 and 44.

9. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:9, 27 and 45.

10. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:10, 28 and 46.

11. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:11, 29 and 47.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

12. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:12, 30 and 48.

13. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:13, 31 and 49.

14. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:14, 32 and 50.

15. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:15, 33 and 51.

16. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:16, 34 and 52.

17. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:17, 35 and 53.

18. Claims: 1-6 all partially.

As invention 1 but concerning Seq.ID:18, 36 and 54.